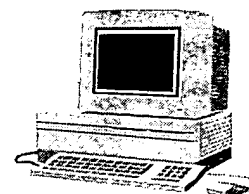


# BioTech-Chem Library

## Search Results

### Feedback Form (Optional)



Scientific & Technical Information Center

The search results generated for your recent request are attached. If you have any questions or comments (compliments or complaints) about the scope or the results of the search, please contact *the BioTech-Chem searcher* who conducted the search *or contact*:

**Mary Hale, Supervisor, 308-4258**  
CM-1 Room 1E01

---

#### *Voluntary Results Feedback Form*

➤ *I am an examiner in Workgroup:* (Example: 1610)

➤ *Relevant prior art found, search results used as follows:*

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

*Types of relevant prior art found:*

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature  
(journal articles, conference proceedings, new product announcements etc.)

➤ *Relevant prior art not found:*

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Search results were not useful in determining patentability or understanding the invention.

**Other Comments:**

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Drop off completed forms at the **Circulation Desk CM-1**, or send to Mary Hale, **CM1-1E01** or e-mail **mary.hale@uspto.gov**.

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 09:53:57 ON 05 MAR 2003

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FILE COVERS 1907 - 5 Mar 2003 VOL 138 ISS 10

FILE LAST UPDATED: 4 Mar 2003 (20030304/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot 159

L59 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2003:5786 HCAPLUS

DN 138:49952

TI Use of **sodium channel blockers** and aspirin  
in manufacturing drugs for producing analgesia synergistically in mammals

IN **Ku, Baoshan; Shum, Hay Kong**

PA Wex Medical Instrumentation Co., Ltd., Peop. Rep. China

SO PCT Int. Appl., 11 pp.

CODEN: PIXXD2

DT Patent

LA Chinese

IC ICM A61K031-517

ICS A61K031-616; A61P025-04; A61P029-00

CC 1-11 (Pharmacology)

FAN.CNT 1

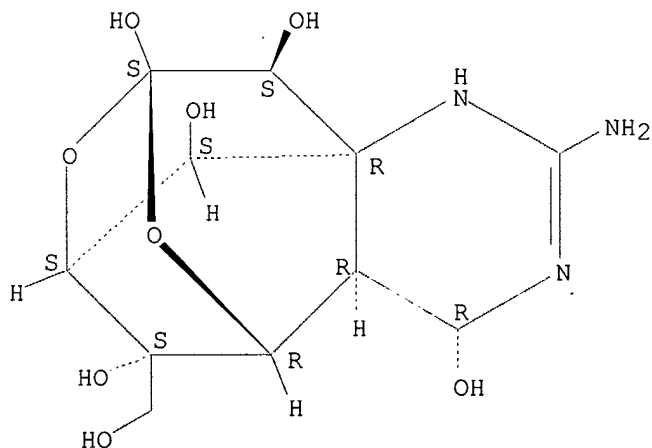
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PI	WO 2003000268	A1	20030103	WO 2002-CN428	20020618
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, AX, AY, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CN 1393223	A	20030129	CN 2001-115990	20010622
PRAI	CN 2001-115990	A	20010622		

AB The present invention relates to the use of combinations of **sodium channel blocking** compds. and aspirin in manufg. drugs for producing synergistically analgesic effect in mammals, in which said compds. bind to .alpha.-subunit of SS1 or SS2 sites in the **sodium channel**. According to the invention, pharmaceutical compns. have enhancing analgesic effect, and therefore dosage of aspirin as well as its side effects would be reduced.

ST **sodium channel blocker** aspirin synergistic

- interaction analgesic
- IT **Ion channel blockers**  
(sodium; use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)
- IT Drug interactions  
(synergistic; use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)
- IT Analgesia  
Analgesics  
(use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)
- IT **Sodium channel**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(.alpha.-subunit of SS1 or SS2; use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)
- IT 7440-23-5, **Sodium**, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(transport; use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)
- IT 50-78-2, Aspirin **4368-28-9**, TTX  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)
- IT **4368-28-9**, TTX  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(use of **sodium channel blockers** and aspirin in manufg. drugs for producing analgesia synergistically in mammals)
- RN 4368-28-9 HCAPLUS
- CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AN 2002:905867 HCAPLUS  
 DN 137:363099  
 TI Analgesic **composition** and method  
 IN Ku, Baoshan; Shum, Frank Hay Kong  
 PA Wex Medical Instrumentation Co., Ltd., Peop. Rep. China  
 SO PCT Int. Appl., 35 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-517  
 ICS A61K031-485; A61P025-04  
 CC 1-11 (Pharmacology)  
 Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002094272	A1	20021128	WO 2002-CN339	20020520
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CN 1386505	A	20021225	CN 2001-118098	20010518
	US 2002198226	A1	20021226	US 2002-62483	20020205
PRAI	CN 2001-118098	A	20010518		

AB A pharmaceutical analgesic **compn. comprising** an **opioid** analgesic agent and a compd. that binds to the **SS1** or **SS2** subunit of a **sodium channel**, such as **tetrodotoxin** and **saxitoxin**, and analogs thereof. Administration of an **opioid** analgesic agent and a compd. that binds to the **SS1** or **SS2** subunit of a **sodium channel**, such as **tetrodotoxin** and **saxitoxin**, and their analogs, produces analgesia in the treatment of pain in mammals. For example, the **synergistic** analgesia effect produced by co-administering **tetrodotoxin** (TTX) and **morphine** was obsd. in a formalin test in rats. **Morphine** used alone at 0.30 mg/kg only produced 10.2% inhibition of formalin-induced pain. **Combination** of TTX at 0.19 .mu.g/kg with **morphine** at 2.50 mg/kg **increased** the inhibition rate to 86.7% from 34.9% where the latter was used alone. TTX at a dose of 0.39 .mu.g/kg (1/50 of LD50) produced an inhibition rate of 32.9% when used alone and 66.2% in **combination** with 0.15 mg/kg of **morphine**, whereas the latter only produced an inhibition rate of 7.2% when used alone.

ST **opioid sodium channel blocker**  
 injection **synergistic** analgesic

IT **Sodium channel**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (**SS1** or **SS2** subunit; **synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)

IT Drug delivery systems  
 (injections, i.m.; **synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)

IT Drug delivery systems  
 (injections, intrathecal; **synergistic** analgesic activity of **combination** of **opioid** and **sodium channel blocker**)

IT Ion channel blockers  
(sodium; synergistic analgesic activity of  
combination of opioid and sodium  
channel blocker)

IT Analgesics  
(synergistic analgesic activity of combination of  
opioid and sodium channel blocker  
)

IT Opioids  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(synergistic analgesic activity of combination of  
opioid and sodium channel blocker  
)

IT Drug interactions  
(synergistic; synergistic analgesic activity of  
combination of opioid and sodium  
channel blocker)

IT 52-26-6, Morphine hydrochloride 57-27-2,  
Morphine, biological studies 76-57-3, Codeine  
76-99-3, Methadone 437-38-7, Fentanyl  
3270-35-7, Tetradonic acid 4368-28-9  
, Tetradotoxin 7724-38-1, Tetradaminotoxin  
7724-39-2, Methoxytetradotoxin 7724-40-5,  
Ethoxytetradotoxin 7724-41-6, Deoxytetradotoxin  
13072-89-4, Anhydrotetradotoxin 35523-89-8,  
Saxitoxin  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(synergistic analgesic activity of combination of  
opioid and sodium channel blocker  
)

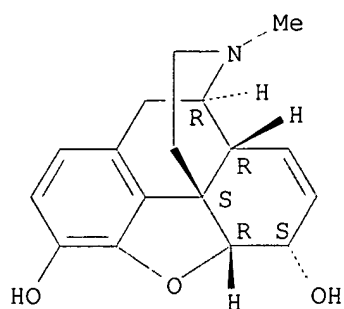
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

(1) Anon; US 4022899 1977 HCAPLUS  
(2) Anon; CN 1145225 A 1997 HCAPLUS  
(3) Xur, Y; JIANGSU CLINICAL MEDICAL JOURNAL 2001, V5(5), P361

IT 52-26-6, Morphine hydrochloride 57-27-2,  
Morphine, biological studies 76-57-3, Codeine  
76-99-3, Methadone 437-38-7, Fentanyl  
3270-35-7, Tetradonic acid 4368-28-9  
, Tetradotoxin 7724-38-1, Tetradaminotoxin  
7724-39-2, Methoxytetradotoxin 7724-40-5,  
Ethoxytetradotoxin 7724-41-6, Deoxytetradotoxin  
13072-89-4, Anhydrotetradotoxin 35523-89-8,  
Saxitoxin  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(synergistic analgesic activity of combination of  
opioid and sodium channel blocker  
)

RN 52-26-6 HCAPLUS  
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-  
(5.alpha.,6.alpha.)-, hydrochloride (9CI) (CA INDEX NAME)

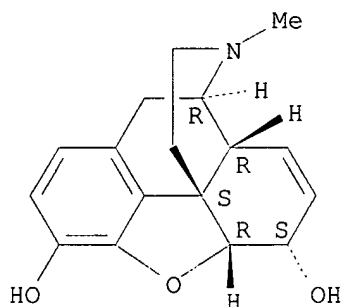
Absolute stereochemistry. Rotation (-).



● HCl

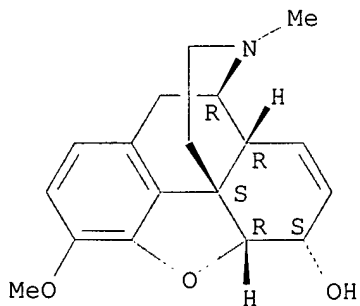
RN 57-27-2 HCAPLUS  
 CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-  
 (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

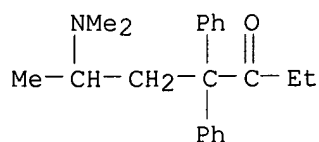


RN 76-57-3 HCAPLUS  
 CN Morphinan-6-ol, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-,  
 (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

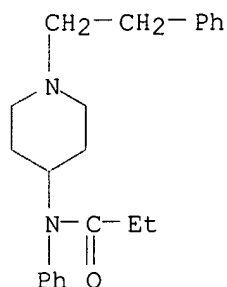


RN 76-99-3 HCAPLUS  
 CN 3-Heptanone, 6-(dimethylamino)-4,4-diphenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



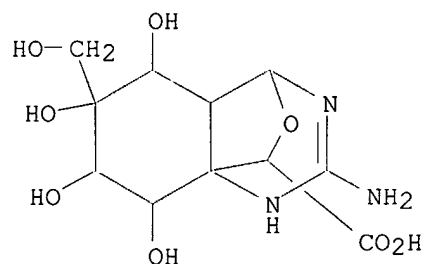
RN 437-38-7 HCAPLUS

CN Propanamide, N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 3270-35-7 HCAPLUS

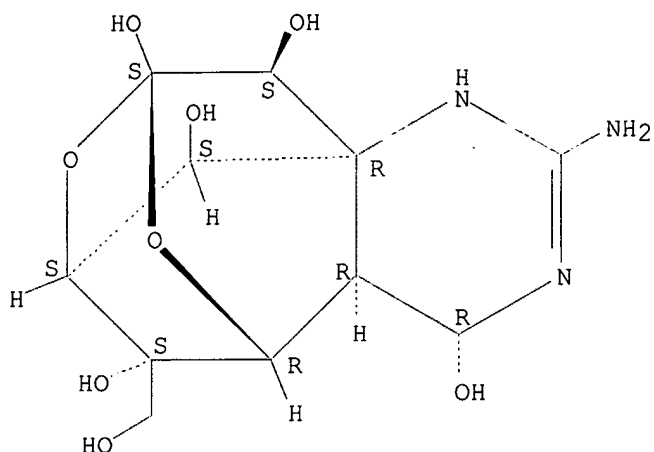
CN 1H-4,8a-(Epoxyethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, (4S,4aR,5R,6S,7R,8R,8aR,9R)- (9CI) (CA INDEX NAME)



RN 4368-28-9 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

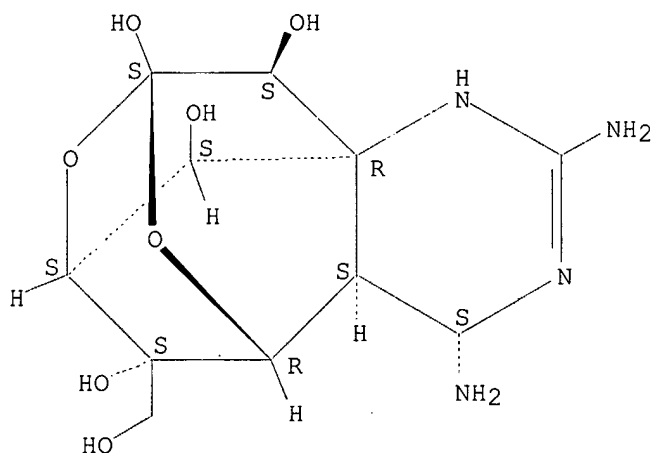
Absolute stereochemistry.



RN 7724-38-1 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-aminooctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

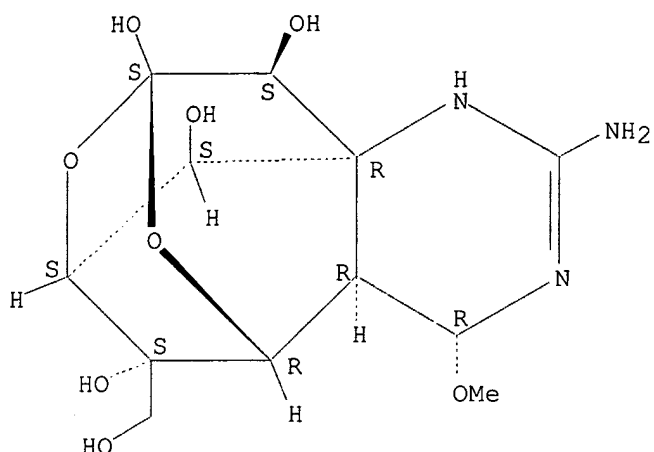


RN 7724-39-2 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, octahydro-12-(hydroxymethyl)-2-imino-4-methoxy-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

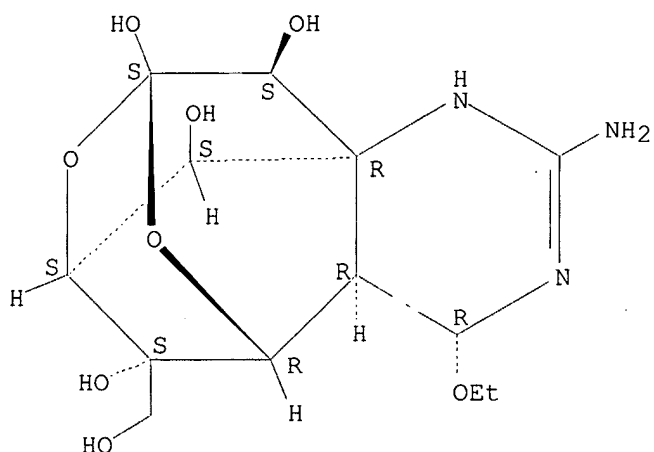




RN 7724-40-5 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-ethoxyoctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S) - (9CI) (CA INDEX NAME)

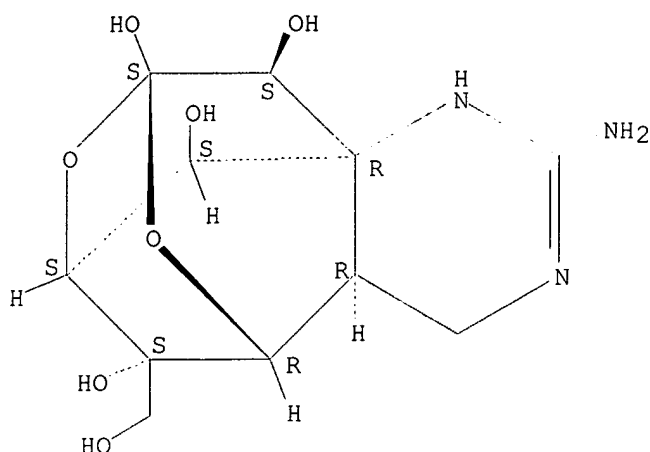
Absolute stereochemistry.



RN 7724-41-6 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4aR,5R,7S,9S,10S,10aR,11S,12S) - (9CI) (CA INDEX NAME)

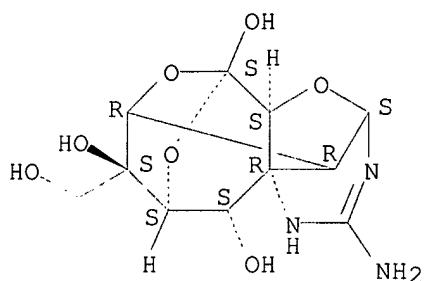
Absolute stereochemistry.



RN 13072-89-4 HCAPLUS

CN 6,10-Epoxy-4,8,11a-metheno-11aH-oxocino[4,3-f][1,3,5]oxadiazepine-6,9,11-triol, 2-amino-1,4,5a,6,8,9,10,11-octahydro-9-(hydroxymethyl)-, (4S,5aS,6S,8R,9S,10S,11S,11aR,12R)- (9CI) (CA INDEX NAME)

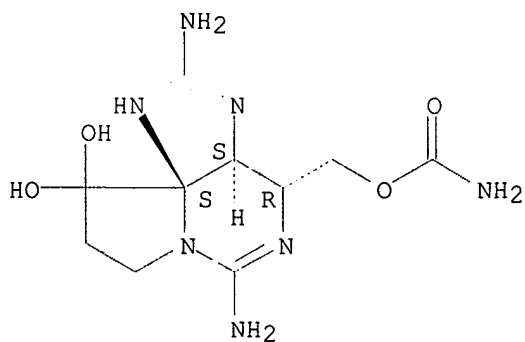
Absolute stereochemistry.



RN 35523-89-8 HCAPLUS

CN 1H,10H-Pyrrolo[1,2-c]purine-10,10-diol, 2,6-diamino-4-[[[(aminocarbonyl)oxy]methyl]-3a,4,8,9-tetrahydro-, (3aS,4R,10aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:408544 HCAPLUS

DN 136:406875

TI Pharmaceutical injections containing **sodium channel blocking** compounds  
 IN Kang, Yuhong; **Shum, Frank Haykong**  
 PA Nanning Maple Leaf Pharmaceutical Co., Ltd., Peop. Rep. China  
 SO PCT Int. Appl., 60 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K045-00  
 ICS A61K031-4995; A61K031-519  
 CC 63-6 (Pharmaceuticals)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002041915	A1	20020530	WO 2001-CN1566	20011119
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1353990	A	20020619	CN 2000-132672	20001122
	US 2002119987	A1	20020829	US 2001-819796	20010329
	AU 2002021491	A5	20020603	AU 2002-21491	20011119
PRAI	CN 2000-132672	A	20001122		
	WO 2001-CN1566	W	20011119		

AB The compn. of the present invention comprises a **sodium channel blocking** compd. which is capable of specifically binding to a site, either on an SS1 region or an SS2 region, on an extracellular region of a **sodium channel** alpha subunit, and a pharmaceutically acceptable carrier. An injection contained **tetrodotoxin** 1.5, 0.5% acetic acid 0.1, propylene glycol 80, and water for injection 100 mL. Stability of **tetrodotoxin** against light, heat, and storage time was studied.

ST pharmaceutical injection **sodium channel blocker**; **tetrodotoxin** acetic acid propylene glycol pharmaceutical injection

IT Quaternary ammonium compounds, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (alkylbenzyl dimethyl, chlorides; pharmaceutical injections contg. **sodium channel blocking** compds.)

IT Drug delivery systems  
 (injections; pharmaceutical injections contg. **sodium channel blocking** compds.)

IT Anti-inflammatory agents  
 (nonsteroidal; pharmaceutical injections contg. **sodium channel blocking** compds.)

IT Acids, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (org.; pharmaceutical injections contg. **sodium channel blocking** compds.)

IT Antibiotics  
 Buffers  
 Permeation enhancers  
 Vasoconstrictors  
 (pharmaceutical injections contg. **sodium channel blocking** compds.)

IT Amines, biological studies  
 Steroids, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical injections contg. **sodium channel blocking compds.**)

IT **Ion channel blockers**  
(**sodium**; pharmaceutical injections contg. **sodium channel blocking compds.**)

IT **4368-28-9, Tetrodotoxin**  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical injections contg. **sodium channel blocking compds.**)

IT 55-68-5, Phenylmercuric nitrate 56-81-5, Glycerine, biological studies  
57-15-8, Chlorobutanol 57-55-6, Propylene glycol, biological studies  
62-38-4, Phenylmercuric acetate 64-19-7, Acetic acid, biological studies  
69-65-8, Mannitol 77-92-9, Citric acid, biological studies 107-21-1, 1,2-Ethanediol, biological studies 112-80-1, Oleic acid, biological studies 126-44-3, Citrate, biological studies 3270-35-7, **Tetrodonic acid** 7647-01-0, Hydrochloric acid, biological studies 7647-14-5, **Sodium chloride**, biological studies 7724-38-1, **Tetrodaminotoxin** 7724-39-2, **Methoxytetrodotoxin** 7724-40-5, **Ethoxytetrodotoxin** 7724-41-6, **Deoxytetrodotoxin** 13072-89-4, **Anhydrotetrodotoxin** 14213-97-9, Borate 14265-44-2, Phosphate, biological studies 35523-89-8, **Saxitoxin**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) ✓  
(pharmaceutical injections contg. **sodium channel blocking compds.**)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

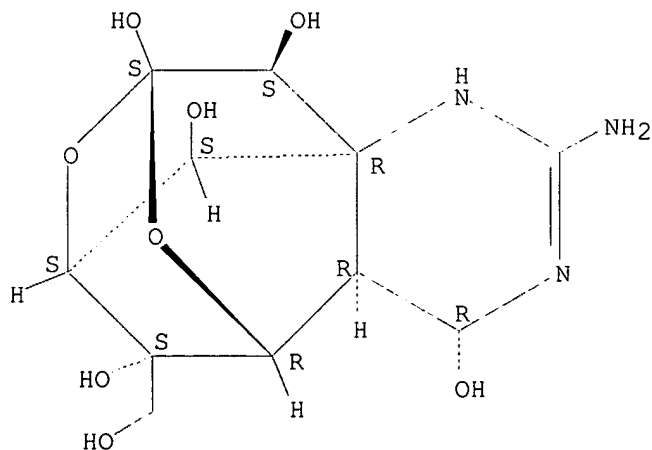
RE  
(1) Anon; US 3898339 A 1975 HCAPLUS  
(2) Anon; WO 9524903 A 1995 HCAPLUS  
(3) Anon; CN 1192903 A 1998 HCAPLUS  
(4) Anon; US 6030974 A 2000 HCAPLUS

IT **4368-28-9, Tetrodotoxin**  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical injections contg. **sodium channel blocking compds.**)

RN 4368-28-9 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

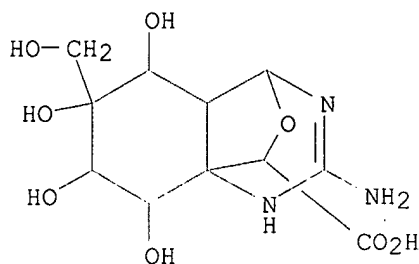


IT 3270-35-7, Tetrodonic acid 7724-38-1  
 , Tetrodaminotoxin 7724-39-2,  
 Methoxytetrodotoxin 7724-40-5,  
 Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin  
 13072-89-4, Anhydrotetrodotoxin 35523-89-8,  
 Saxitoxin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pharmaceutical injections contg. **sodium channel**  
**blocking** compds.)

RN 3270-35-7 HCAPLUS

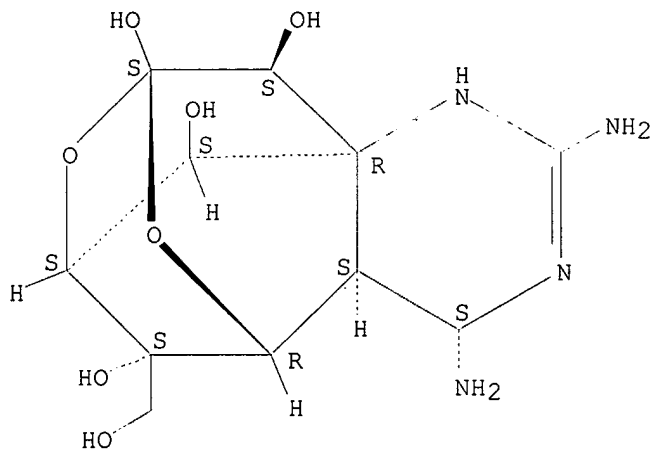
CN 1H-4,8a-(Epoxy-methano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-  
 hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-,  
 (4S,4aR,5R,6S,7R,8R,8aR,9R)- (9CI) (CA INDEX NAME)



RN 7724-38-1 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-  
 tetrol, 4-amino-octahydro-12-(hydroxymethyl)-2-imino-,  
 (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

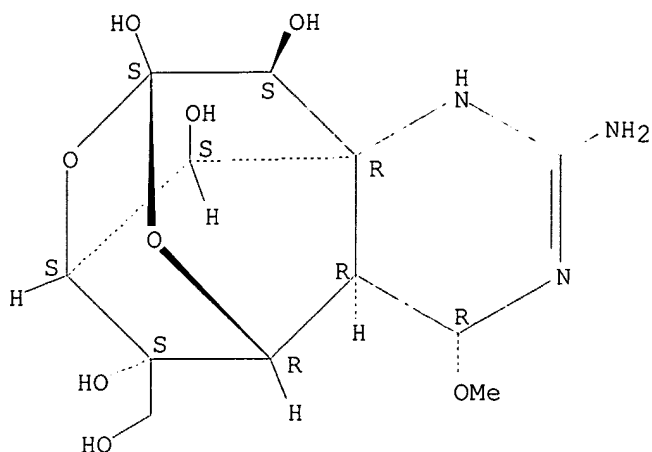
Absolute stereochemistry.



RN 7724-39-2 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-  
 tetrol, octahydro-12-(hydroxymethyl)-2-imino-4-methoxy-,  
 (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

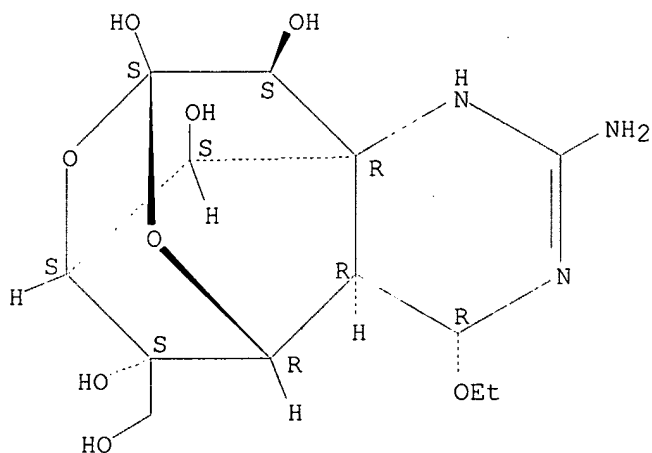
Absolute stereochemistry.



RN 7724-40-5 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-ethoxyoctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

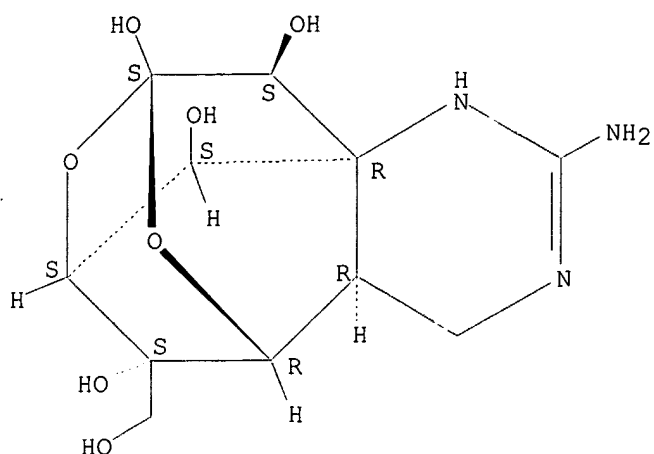
Absolute stereochemistry.



RN 7724-41-6 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

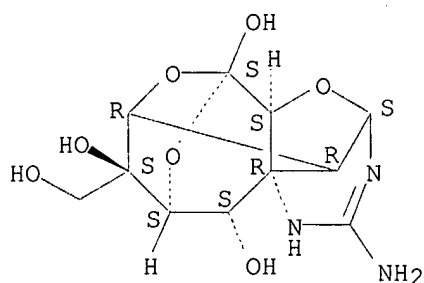
Absolute stereochemistry.



RN 13072-89-4 HCAPLUS

CN 6,10-Epoxy-4,8,11a-metheno-11aH-oxocino[4,3-f][1,3,5]oxadiazepine-6,9,11-triol, 2-amino-1,4,5a,6,8,9,10,11-octahydro-9-(hydroxymethyl)-, (4S,5aS,6S,8R,9S,10S,11S,11aR,12R)- (9CI) (CA INDEX NAME)

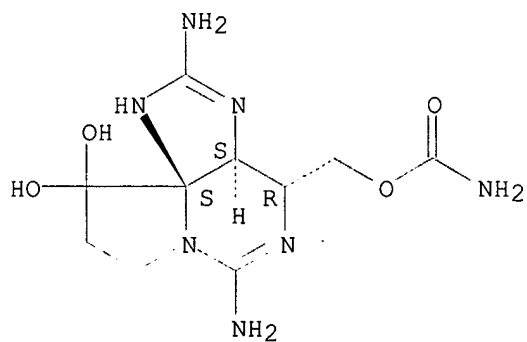
Absolute stereochemistry.



RN 35523-89-8 HCAPLUS

CN 1H,10H-Pyrrolo[1,2-c]purine-10,10-diol, 2,6-diamino-4-[[ (aminocarbonyl)oxy]methyl]-3a,4,8,9-tetrahydro-, (3aS,4R,10aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:220374 HCAPLUS

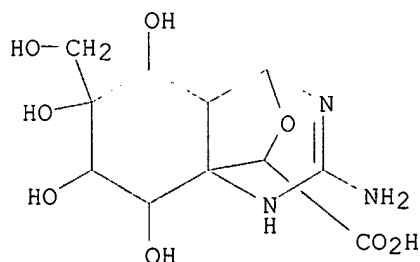
DN 136:241691

TI A method of analgesia using **sodium channel blockers**  
 IN Dong, Qingbin; Shum, Frank Haykong  
 PA WEX Medical Instrumentation Co., Peop. Rep. China  
 SO PCT Int. Appl., 60 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-517  
 ICS A61P023-02; A61P025-04  
 CC 1-11 (Pharmacology)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002022129	A1	20020321	WO 2001-CN1391	20010911
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1356104	A	20020703	CN 2000-124517	20000918
	US 6407088	B1	20020618	US 2000-695053	20001025
	AU 2002013785	A5	20020326	AU 2002-13785	20010911
PRAI	CN 2000-124517	A	20000918		
	WO 2001-CN1391	W	20010911		
AB	This invention relates to a method of producing analgesia in a mammal experiencing pain by systemically administering an effective amt. of a compn. comprising essentially of a <b>sodium channel blocking</b> compd., in a suitable pharmaceutical vehicle, to alleviate the pain.				
ST	pain neuropathic cancer analgesia <b>sodium channel blocker</b>				
IT	Drug delivery systems (aerosols; analgesia using <b>sodium channel blockers</b> for neuropathic and cancer pain)				
IT	Analgesics Behavior Drug withdrawal Human (analgesia using <b>sodium channel blockers</b> for neuropathic and cancer pain)				
IT	Drug delivery systems (implants, osmotic pump; analgesia using <b>sodium channel blockers</b> for neuropathic and cancer pain)				
IT	Collagens, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (implants; analgesia using <b>sodium channel blockers</b> for neuropathic and cancer pain)				
IT	Drug delivery systems (injections, i.m.; analgesia using <b>sodium channel blockers</b> for neuropathic and cancer pain)				
IT	Drug delivery systems (injections, i.v.; analgesia using <b>sodium channel blockers</b> for neuropathic and cancer pain)				
IT	Drug delivery systems (injections, s.c.; analgesia using <b>sodium channel blockers</b> for neuropathic and cancer pain)				
IT	Nerve, disease (neuralgia; analgesia using <b>sodium channel blockers</b> for neuropathic and cancer pain)				



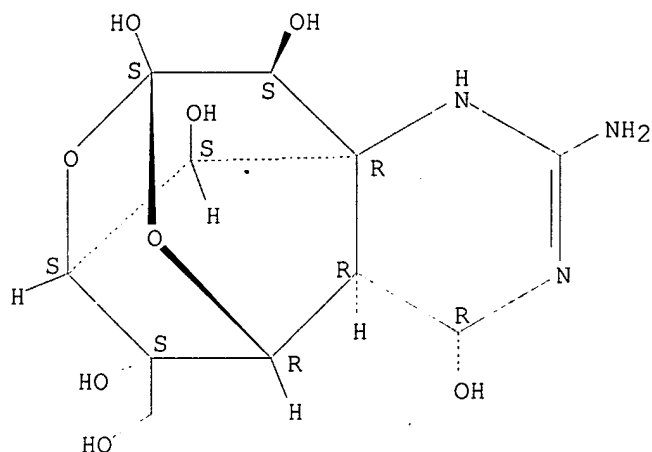
**blockers** for neuropathic and cancer pain)  
 IT Drug delivery systems  
     (oral; analgesia using **sodium channel blockers** for neuropathic and cancer pain)  
 IT Drug delivery systems  
     (osmotic pumps, implants; analgesia using **sodium channel blockers** for neuropathic and cancer pain)  
 IT Neoplasm  
     (pain; analgesia using **sodium channel blockers** for neuropathic and cancer pain)  
 IT **Ion channel blockers**  
     (**sodium**; analgesia using **sodium channel blockers** for neuropathic and cancer pain)  
 IT Drug delivery systems  
     (sublingual; analgesia using **sodium channel blockers** for neuropathic and cancer pain)  
 IT Drug delivery systems  
     (suppositories; analgesia using **sodium channel blockers** for neuropathic and cancer pain)  
 IT Drug delivery systems  
     (tapes; analgesia using **sodium channel blockers** for neuropathic and cancer pain)  
 IT 3270-35-7, **Tetrodonic acid** 4368-28-9  
     , **Tetrodotoxin** 7724-38-1, **Tetrodaminotoxin** 7724-39-2, **Methoxytetrodotoxin** 7724-40-5, **Ethoxytetrodotoxin** 7724-41-6, **Deoxytetrodotoxin** 13072-89-4, **Anhydrotetrodotoxin** 35523-89-8D, **Saxitoxin**, hydroxy derivs. 64296-20-4, **Neosaxitoxin**  
     RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (analgesia using **sodium channel blockers** for neuropathic and cancer pain)  
 RE.CNT 2      THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
 (1) Anon; US 4022899 1977 HCAPLUS  
 (2) Anon; CN 1145225 A 1997 HCAPLUS  
 IT 3270-35-7, **Tetrodonic acid** 4368-28-9  
     , **Tetrodotoxin** 7724-38-1, **Tetrodaminotoxin** 7724-39-2, **Methoxytetrodotoxin** 7724-40-5, **Ethoxytetrodotoxin** 7724-41-6, **Deoxytetrodotoxin** 13072-89-4, **Anhydrotetrodotoxin** 35523-89-8D, **Saxitoxin**, hydroxy derivs.  
     RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (analgesia using **sodium channel blockers** for neuropathic and cancer pain)  
 RN 3270-35-7 HCAPLUS  
 CN 1H-4,8a-(Epoxymethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, (4S,4aR,5R,6S,7R,8R,8aR,9R)- (9CI) (CA INDEX NAME)



RN 4368-28-9 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

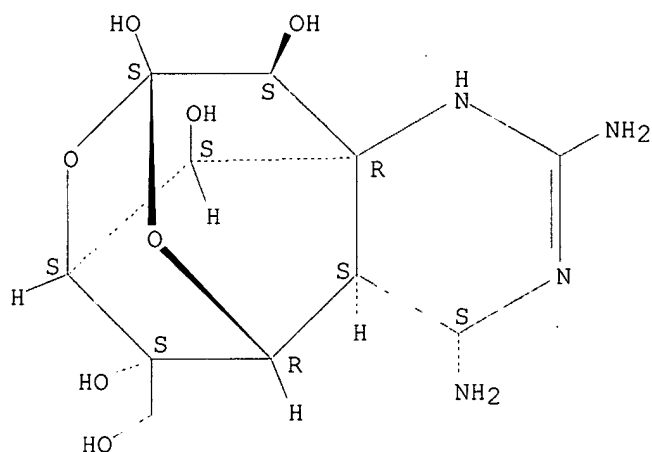
Absolute stereochemistry.



RN 7724-38-1 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-aminooctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

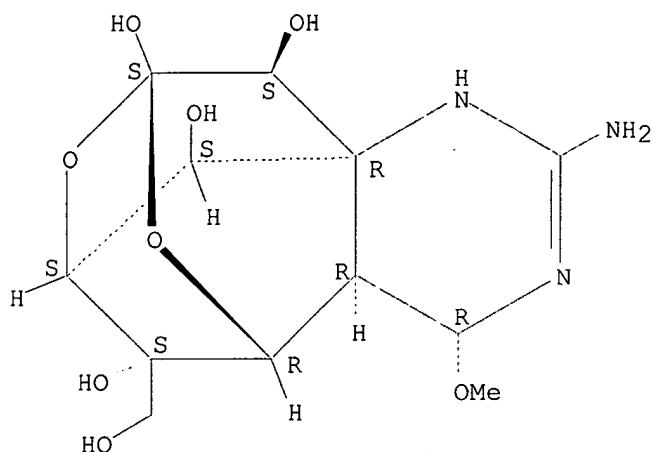
Absolute stereochemistry.



RN 7724-39-2 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, octahydro-12-(hydroxymethyl)-2-imino-4-methoxy-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

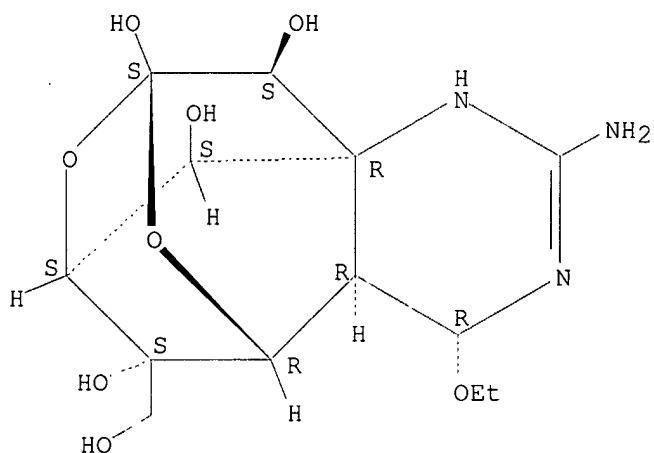
Absolute stereochemistry.



RN 7724-40-5 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-ethoxyoctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)-(9CI) (CA INDEX NAME)

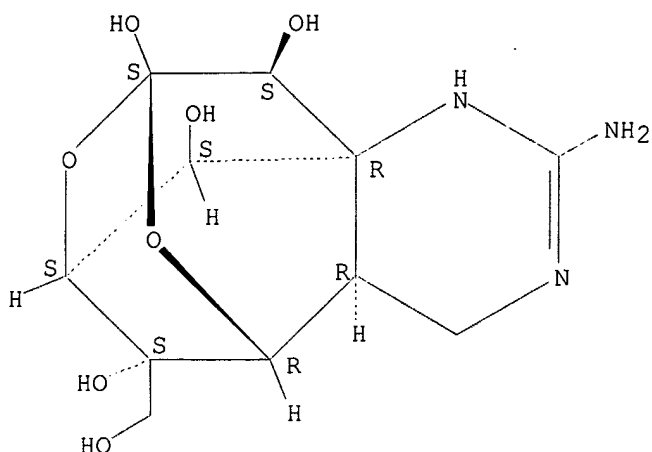
Absolute stereochemistry.



RN 7724-41-6 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4aR,5R,7S,9S,10S,10aR,11S,12S)-(9CI) (CA INDEX NAME)

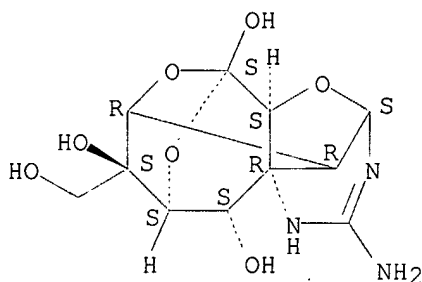
Absolute stereochemistry.



RN 13072-89-4 HCAPLUS

CN 6,10-Epoxy-4,8,11a-metheno-11aH-oxocino[4,3-f][1,3,5]oxadiazepine-6,9,11-triol, 2-amino-1,4,5a,6,8,9,10,11-octahydro-9-(hydroxymethyl)-, (4S,5aS,6S,8R,9S,10S,11S,11aR,12R)- (9CI) (CA INDEX NAME)

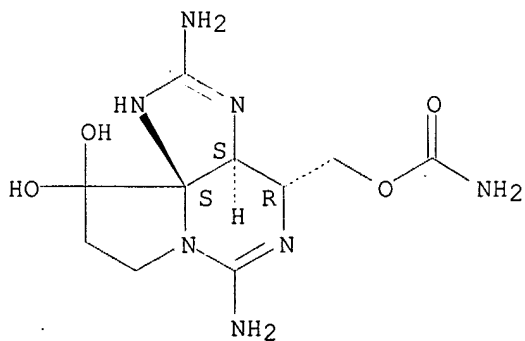
Absolute stereochemistry.



RN 35523-89-8 HCAPLUS

CN 1H,10H-Pyrrolo[1,2-c]purine-10,10-diol, 2,6-diamino-4-[[ (aminocarbonyl)oxy]methyl]-3a,4,8,9-tetrahydro-, (3aS,4R,10aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:220373 HCAPLUS

DN 136:226808

TI A method of local anesthesia and analgesia using **sodium channel blockers** and local anesthetics  
 IN **Ku, Baoshan**; Qi, Shiquan  
 PA WEX Medical Instrumentation Co., Ltd., Peop. Rep. China  
 SO PCT Int. Appl., 25 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-517  
 ICS A61P023-02; A61P029-00  
 CC 1-11 (Pharmacology)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2002022128	A1	20020321	WO 2001-CN1390	20010911	
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
	CN 1343491	A	20020410	CN 2000-124518	20000918	
	AU 2002013784	A5	20020326	AU 2002-13784	20010911	
PRAI	CN 2000-124518	A	20000918			
	WO 2001-CN1390	W	20010911			
AB	The present invention provides a method of producing local analgesia and anesthesia in a mammal experiencing pain in a nerve tissue region. The method includes topically administering to the region, in a suitable pharmaceutical vehicle, an ED of a <b>sodium channel blocking</b> compd. in a pharmaceutically suitable vehicle.					
ST	neuropathic pain local anesthesia analgesia <b>sodium channel blocker</b>					
IT	Analgesics Human (local anesthesia and analgesia using <b>sodium channel blockers</b> and local anesthetics for neuropathic pain)					
IT	Anesthetics (local; local anesthesia and analgesia using <b>sodium channel blockers</b> and local anesthetics for neuropathic pain)					
IT	Nerve, disease (neuralgia; local anesthesia and analgesia using <b>sodium channel blockers</b> and local anesthetics for neuropathic pain)					
IT	Tooth (pulp; local anesthesia and analgesia using <b>sodium channel blockers</b> and local anesthetics for neuropathic pain)					
IT	Nerve (sciatic; local anesthesia and analgesia using <b>sodium channel blockers</b> and local anesthetics for neuropathic pain)					
IT	Ion channel blockers ( <b>sodium</b> ; local anesthesia and analgesia using <b>sodium channel blockers</b> and local anesthetics for neuropathic pain)					
IT	Drug interactions (synergistic; local anesthesia and analgesia using <b>sodium channel blockers</b> and local anesthetics for neuropathic pain)					

IT Drug delivery systems  
(topical; local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)

IT Nerve  
(trigeminal; local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)

IT **4368-28-9, Tetrodotoxin**  
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)

IT 59-46-1, Procaine 94-24-6, Tetracaine 137-58-6, Lidocaine 3270-35-7, Tetrodonic acid 7724-38-1, Tetrodaminotoxin 7724-39-2, Methoxytetrodotoxin 7724-40-5, Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin 13072-89-4, Anhydrotetrodotoxin  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

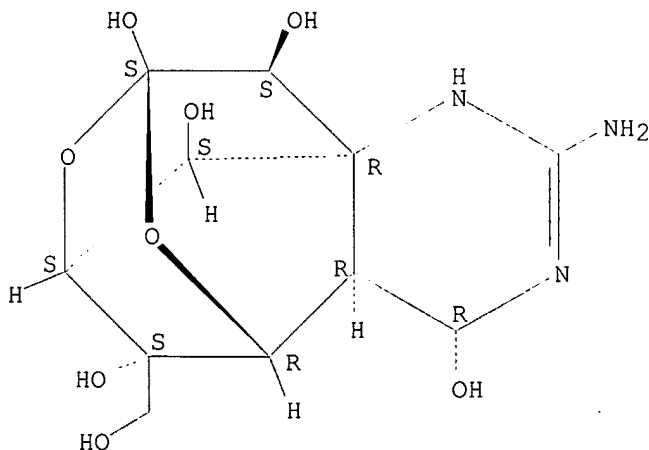
RE  
(1) Anon; CN 1145225 A 1977 HCAPLUS  
(2) Anon; US 4022899 1997 HCAPLUS

IT **4368-28-9, Tetrodotoxin**  
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)

RN 4368-28-9 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

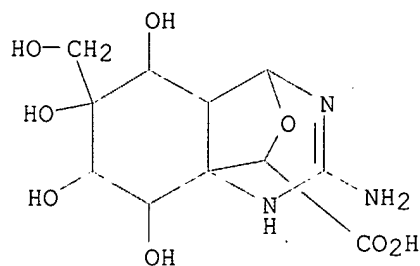


IT **3270-35-7, Tetrodonic acid 7724-38-1**, Tetrodaminotoxin 7724-39-2, Methoxytetrodotoxin 7724-40-5, Ethoxytetrodotoxin 7724-41-6, Deoxytetrodotoxin 13072-89-4, Anhydrotetrodotoxin  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)  
 (local anesthesia and analgesia using **sodium channel blockers** and local anesthetics for neuropathic pain)

RN 3270-35-7 HCAPLUS

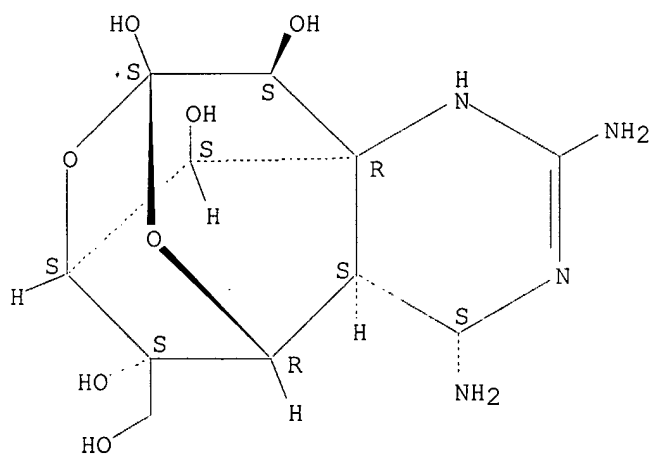
CN 1H-4,8a-(Epoxyethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, (4S,4aR,5R,6S,7R,8R,8aR,9R)- (9CI) (CA INDEX NAME)



RN 7724-38-1 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-aminooctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

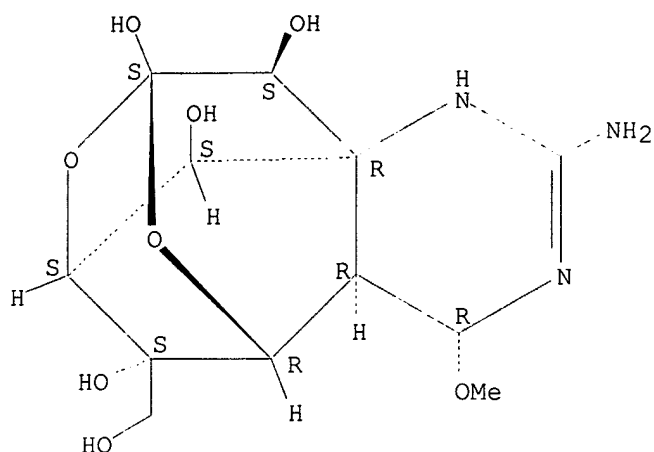
Absolute stereochemistry.



RN 7724-39-2 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, octahydro-12-(hydroxymethyl)-2-imino-4-methoxy-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

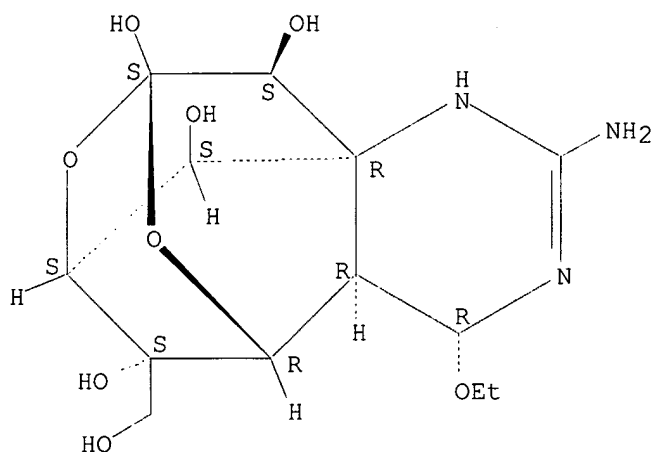
Absolute stereochemistry.



RN 7724-40-5 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-ethoxyoctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

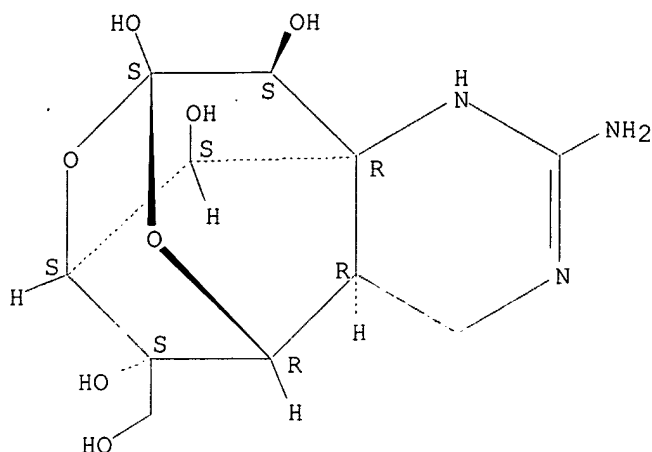


RN 7724-41-6 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4aR,5R,7S,9S,10S,10aR,11S,12S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

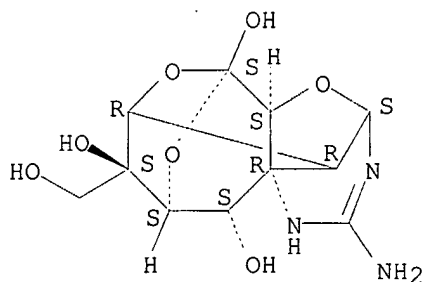




RN 13072-89-4 HCAPLUS

CN 6,10-Epoxy-4,8,11a-metheno-11aH-oxocino[4,3-f][1,3,5]oxadiazepine-6,9,11-triol, 2-amino-1,4,5a,6,8,9,10,11-octahydro-9-(hydroxymethyl)-, (4S,5aS,6S,8R,9S,10S,11S,11aR,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:552385 HCAPLUS

DN 135:316858

TI Nociception and allodynia/hyperalgesia induced by intrathecal administration of fenvalerate

AU Kamei, Junzo; Sasaki, Mitsumasa; Zushida, Ko; Morita, Kayo; Tanaka, Shun-Ichi

CS Department of Pathophysiology & Therapeutics, Faculty of Pharmaceutical Sciences, Hoshi University, Tokyo, 142-8501, Japan

SO Japanese Journal of Pharmacology (2001), 86(3), 336-341

CODEN: JJPAAZ; ISSN: 0021-5198

PB Japanese Pharmacological Society

DT Journal

LA English

CC 14-10 (Mammalian Pathological Biochemistry)

cross-reference(s): 1

intrathecal injection of fenvalerate, a Na channel

blocker, at doses of 0.01 to 3 .mu.g, dose-dependently induced the appearance of a characteristic behavioral syndrome mainly consisting of the hind limb scratching directed towards caudal parts of the body and/or licking of the hind legs in mice. Fenvalerate-induced behavior was inhibited by morphine (1 - 10 mg/kg, i.p.). The scratching behavior was also inhibited by mexiletine, a Na channel blocker; MK-801, a N-methyl-D-aspartate ion-

**channel blocker**; and GR82334, a neurokinin-1-receptor antagonist. Calphostin C (3 pmol, i.t.), a protein kinase C inhibitor, inhibited fenvalerate-induced behavior. On the other hand, phorbol-12, 13-dibutyrate (50 pmol, i.t.), a protein kinase C activator, markedly **enhanced** the fenvalerate-induced behavior. The present results also showed that fenvalerate produced thermal allodynia and hyperalgesia in the tail-flick test. Furthermore, fenvalerate-induced thermal allodynia and hyperalgesia were inhibited by the pretreatment with calphostin C. These results suggest that the intrathecal administration of fenvalerate induces a marked nociceptive response and thermal allodynia/hyperalgesia, and they suggest that **tetrodotoxin**-resistant **Na channels** may play an important role in this effect.

- ST fenvalerate nociception **tetrodotoxin** resistant **sodium channel**
- IT Tachykinin receptors  
(NK1 antagonists; fenvalerate induces nociception and allodynia/hyperalgesia in mice)
- IT Glutamate antagonists  
(NMDA antagonists; fenvalerate induces nociception and allodynia/hyperalgesia in mice)
- IT Pain  
Skin, disease  
(allodynia; fenvalerate induces nociception and allodynia/hyperalgesia in mice)
- IT Pain  
(fenvalerate induces nociception and allodynia/hyperalgesia in mice)
- IT Pain  
(hyperalgesia; fenvalerate induces nociception and allodynia/hyperalgesia in mice)
- IT **Ion channel blockers**  
(**sodium**; fenvalerate induces nociception and allodynia/hyperalgesia in mice)
- IT **Sodium channel**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**tetrodotoxin**-resistant; fenvalerate induces nociception and allodynia/hyperalgesia in mice)
- IT 121263-19-2, Calphostin C  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(effect of pretreatment with, on fenvalerate-induced nociception in mice)
- IT 57-27-2, **Morphine**, biological studies 31828-71-4, Mexiletine 77086-22-7, MK-801 129623-01-4, GR82334  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(effect of, on fenvalerate-induced nociception in mice)
- IT 141436-78-4, Protein kinase C  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(effect of, on fenvalerate-induced nociception in mice)
- IT 51630-58-1, Fenvalerate  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(fenvalerate induces nociception and allodynia/hyperalgesia in mice)
- IT 4368-28-9, **Tetrodotoxin**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**tetrodotoxin**-resistant **Na channel**;  
fenvalerate induces nociception and allodynia/hyperalgesia in mice)

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

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IT 57-27-2, **Morphine**, biological studies

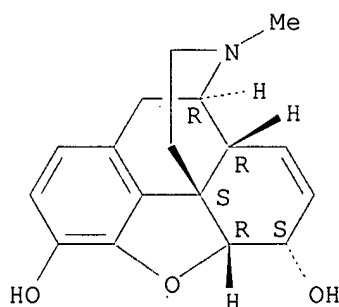
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(effect of, on fenvalerate-induced nociception in mice)

RN 57-27-2 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-  
(5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 4368-28-9, **Tetrodotoxin**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

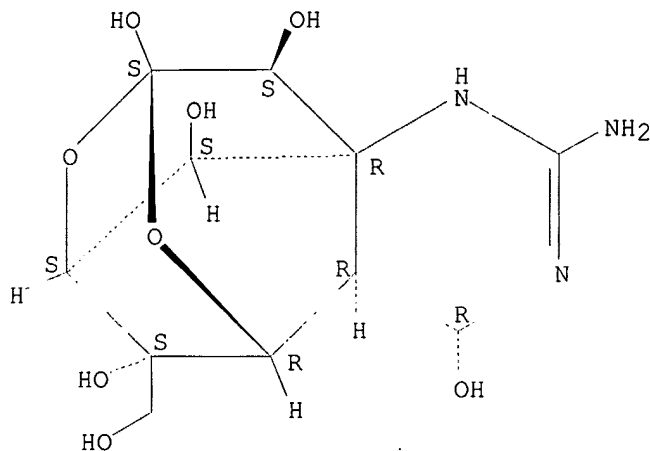
(tetrodotoxin-resistant Na channel;

fenvalerate induces nociception and allodynia/hyperalgesia in mice)

RN 4368-28-9 HCAPLUS

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:489224 HCAPLUS

DN 135:97445

TI Method for relieving pain associated with an internal disease site

IN Luiken, George A.

PA Fluoro Probe, Inc., USA

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001047512	A2	20010705	WO 2000-US42661	20001206
	WO 2001047512	A3	20020502		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-457498 A1 19991208

AB Methods are provided for in vivo administration of a pain-relieving drug, such as a local anesthetic (e.g. lidocaine), to an interior disease site for pain relief at the interior disease site. In the invention pain treatment methods, a subject is administered a targeting construct comprising a biol. compatible pain-relieving agent and a tumor-avid ligand or monoclonal antibody that preponderantly binds to or is taken up by the tissue assocd. with an interior disease site. Administration is by a

method other than topical injection or application, such as parenteral injection. Because the pain-relieving agent is delivered by the ligand to the disease site, intractable pain situated in the interior of the body, such as is caused by various tumors, can be managed using a lower level of the pain-relieving agent then is required when the pain-relieving agent is injected in the free state.

ST tumor targeting pain relieving antibody conjugate

IT Chromogranins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(A; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(CA 15-3, antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Immunoglobulin receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(IgE type II, antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(TAG-72 (tumor-assocd. glycoprotein 72), antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT CA 125 (carbohydrate antigen)

CA19-9 antigen

CD19 (antigen)

CD20 (antigen)

CD22 (antigen)

CD45 (antigen)

CD5 (antigen)

Carcinoembryonic antigen

Epidermal growth factor receptors

Estrogen receptors

Mucins

Progesterone receptors

Prostate-specific antigen

.alpha.-Fetoproteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT CD30 (antigen)

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Peptides, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(binding hormone receptors, ligands; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Toxoids

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(botulin; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Gene, animal

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(c-erbB2, antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Antiarrhythmics

(class I; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Intestine, neoplasm

(colon; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Intestine, neoplasm  
(colorectal; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Immunoglobulins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(fragments; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Drug delivery systems  
(injections, i.v.; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Anesthetics  
(local; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Antibodies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monoclonal; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Bladder  
Endocrine system  
Head  
Mammary gland  
Neck, anatomical  
Pituitary gland  
Prostate gland  
(neoplasm; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Nerve, neoplasm  
(neuroblastoma; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Endocrine system  
(neuroendocrine system, neoplasm; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Lymphoma  
(non-Hodgkin's; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Lung, neoplasm  
(non-small-cell carcinoma; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Analgesia  
Anticonvulsants  
Brain, neoplasm  
Carcinoid  
Drug targeting  
Hodgkin's disease  
Liver, neoplasm  
Melanoma  
Multiple myeloma  
Nicotinic agonists  
Ovary, neoplasm  
Pancreas, neoplasm  
Sarcoma  
Testis, neoplasm  
Thyroid gland, neoplasm  
Uterus, neoplasm  
(pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Hormones, animal, biological studies  
**Opioids**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Growth hormone receptors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptides binding to, ligands; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Lung, neoplasm  
(small-cell carcinoma; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT **Ion channel blockers**  
(sodium; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Antigens  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(tumor-assocd., antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(tumor-specific, antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 9002-61-3, Human chorionic gonadotropin  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(antibody to; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 69-78-3 2831-66-5 68181-17-9 72252-96-1 106145-13-5 115616-51-8  
150244-18-1 158913-22-5 160854-54-6 204713-28-0  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(crosslinking agent; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 329900-75-6  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 7658-08-4 51110-01-1, Somatostatin  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ligand; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 2543-43-3 130838-28-7 150243-58-6 150243-59-7 153177-60-7  
256504-33-3 256504-34-4 256504-35-5 256504-36-6  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(linker moiety; pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

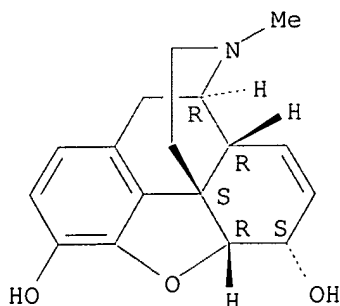
IT **57-27-2, Morphine**, biological studies 57-42-1,  
Meperidine 59-46-1, Procaine 63-68-3, Methionine, biological studies  
76-42-6, Oxycodone **76-99-3, Methadone** 85-79-0,  
Dibucaine 94-24-6, Tetracaine 96-88-8, Mepivacaine 125-28-0,  
Dihydrocodeine 125-29-1, Hydrocodone 133-16-4, Chloroprocaine  
136-47-0 137-58-6, Lidocaine 466-99-9, Hydromorphone 509-60-4,  
Dihydromorphone 561-27-3, Heroin 721-50-6, Prilocaine 22264-50-2,  
1-aminocyclobutane-1-carboxylic acid 36637-18-0, Etidocaine  
38396-39-3, Bupivacaine 52485-79-7, Buprenorphine 60142-96-3,  
Gabapentin 66532-85-2, Propacetamol 83150-76-9, Octreotide  
84057-95-4, Ropivacaine 107452-89-1, Ziconotide 108736-35-2,  
Lanreotide 113775-47-6, Dexmedetomidine 161982-62-3, P829  
264596-75-0, P587  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT **57-27-2, Morphine**, biological studies **76-99-3, Methadone**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

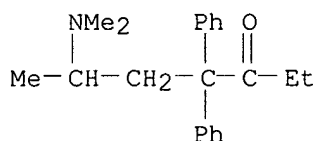
RN 57-27-2 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-  
(5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 76-99-3 HCAPLUS  
 CN 3-Heptanone, 6-(dimethylamino)-4,4-diphenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L59 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1992:440075 HCAPLUS  
 DN 117:40075  
 TI Cardiac instability amplified by use-dependent **sodium channel blockade**  
 AU Starmer, C. Frank; Lancaster, Alisa R.; Lastra, Anselmo A.; Grant, Augustus O.  
 CS Med. Cent., Duke Univ., Durham, NC, 27710, USA  
 SO American Journal of Physiology (1992), 262(4, Pt. 2), H1305-H1310  
 CODEN: AJPHAP; ISSN: 0002-9513  
 DT Journal  
 LA English  
 CC 1-8 (Pharmacology)  
 AB Drugs that exhibit use-dependent **Na channel blockade**, including antiarrhythmic agents, tricyclic antidepressants, **opiate**-like analgesics, and cocaine, are linked with an increased susceptibility to cardiac arrhythmias and sudden death. Computer simulations indicate that **Na channel blockade** retards recovery of excitability, thereby increasing the spatial dispersion of refractoriness, a precursor of many cardiac arrhythmias. In isolated rabbit left atria, stimuli timed to occur at increasing intervals following conditioning stimuli reveal an unstable interval (vulnerable period) during which single stimuli initiate trains of responses. The vulnerable period is extended by use-dependent **Na channel blockade** and provides a model for assaying proarrhythmic potential and probing cardiac instability.  
 ST heart arrhythmia **sodium channel blocker**  
 IT **Opioids**  
 RL: BIOL (Biological study)  
 (analgesics, heart arrhythmia induction by, mechanism of)  
 IT Antiarrhythmics  
 (heart arrhythmia from, evaluation of)  
 IT Toxicity  
 (of drugs, heart arrhythmia in, mechanism of)  
 IT Analgesics



(**opiates**, heart arrhythmia induction by, mechanism of)  
IT Antidepressants  
(tricyclic, heart arrhythmia induction by, mechanism of)  
IT Heart, disease  
(arrhythmia, from **sodium channel blockers**  
, mechanism of)  
IT **Ion channel blockers**  
(**sodium**, heart arrhythmia from, mechanism of)  
IT 50-36-2, Cocaine 137-58-6, Lidocaine  
RL: BIOL (Biological study)  
(heart arrhythmia from, evaluation of)

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DICTIONARY FILE UPDATES: 3 MAR 2003 HIGHEST RN 496834-05-0

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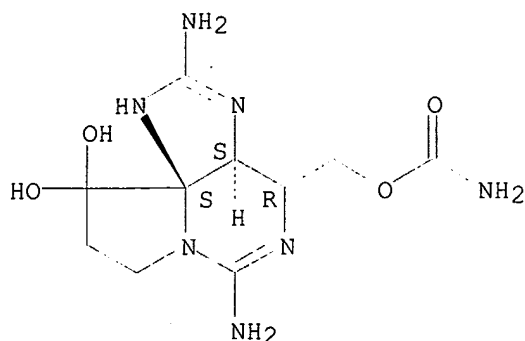
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d ide can tot 160

L60 ANSWER 1 OF 13 REGISTRY COPYRIGHT 2003 ACS  
RN 35523-89-8 REGISTRY  
CN 1H,10H-Pyrrolo[1,2-c]purine-10,10-diol, 2,6-diamino-4-  
[[aminocarbonyl)oxy)methyl]-3a,4,8,9-tetrahydro-, (3aS,4R,10aS)- (9CI)  
(CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H,10H-Pyrrolo[1,2-c]purine-10,10-diol, 2,6-diamino-4-  
[[aminocarbonyl)oxy)methyl]-3a,4,8,9-tetrahydro-, [3aS-  
(3a.alpha.,4.alpha.,10aR\*)]-  
CN Saxitoxin (7CI, 8CI)  
OTHER NAMES:  
CN (+)-Saxitoxin  
CN Saxitoxin hydrate  
CN STX  
FS STEREOSEARCH  
DR 11017-04-2, 55803-44-6, 51938-46-6  
MF C10 H17 N7 O4  
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BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CEN, CSCHEM, DDFU, DRUGU,  
EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, NAPRALERT, NIOSHTIC, PROMT,  
RTECS\*, TOXCENTER, ULIDAT, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

798 REFERENCES IN FILE CA (1962 TO DATE)  
 38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 799 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:132294  
 REFERENCE 2: 138:132287  
 REFERENCE 3: 138:118720  
 REFERENCE 4: 138:118718  
 REFERENCE 5: 138:102233  
 REFERENCE 6: 138:102105  
 REFERENCE 7: 138:88656  
 REFERENCE 8: 138:84812  
 REFERENCE 9: 138:83128  
 REFERENCE 10: 138:34253

L60 ANSWER 2 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 13072-89-4 REGISTRY

CN 6,10-Epoxy-4,8,11a-metheno-11aH-oxocino[4,3-f][1,3,5]oxadiazepine-6,9,11-triol, 2-amino-1,4,5a,6,8,9,10,11-octahydro-9-(hydroxymethyl)-, (4S,5aS,6S,8R,9S,10S,11S,11aR,12R)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Tetrodotoxin, 4,9-anhydro- (8CI)

CN Tetrodotoxin, 4,9-dideoxy-4,9-epoxy-, (4.beta.,9.beta.)-

CN Tetrodotoxin, anhydro- (7CI)

OTHER NAMES:

CN 4,9-Anhydrotetrodotoxin

CN Anhydroepitetrodotoxin

CN Anhydrotetrodotoxin

FS STEREOSEARCH

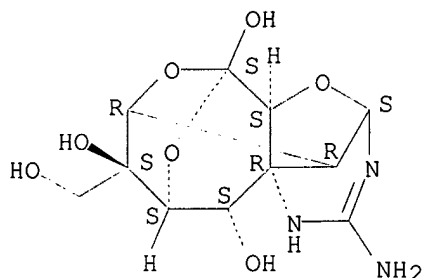
DR 7724-36-9, 16998-61-1, 17289-89-3, 2054-43-5

MF C11 H15 N3 O7

CI COM

LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, CA, CAOLD, CAPLUS,  
CASREACT, MEDLINE, NAPRALERT, RTECS\*, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

85 REFERENCES IN FILE CA (1962 TO DATE)  
85 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:38538  
REFERENCE 2: 137:363099  
REFERENCE 3: 137:336926  
REFERENCE 4: 137:304801  
REFERENCE 5: 137:227949  
REFERENCE 6: 137:180989  
REFERENCE 7: 137:92915  
REFERENCE 8: 137:63423  
REFERENCE 9: 137:58860  
REFERENCE 10: 137:1763

L60 ANSWER 3 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN **7724-41-6** REGISTRY

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 2-amino-1,4,4a,5,9,10-hexahydro-12-(hydroxymethyl)-, (4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, octahydro-12-(hydroxymethyl)-2-imino-, [4aR-(4a.alpha.,5.alpha.,7.alpha.,9.alpha.,10.alpha.,10a.beta.,11S\*,12S\*)]-

CN Tetrodotoxin, 4-deoxy- (8CI)

CN Tetrodotoxin, deoxy- (7CI)

OTHER NAMES:

CN Deoxytetrodotoxin

CN Desoxytetrodotoxin

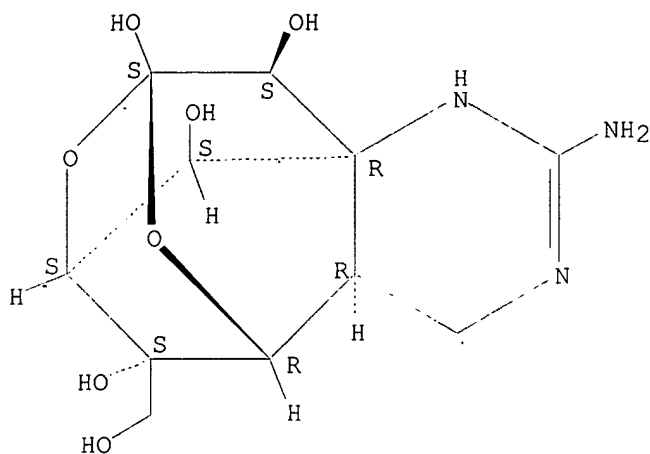
FS STEREOSEARCH

DR 16813-05-1, 17289-92-8

MF C11 H17 N3 O7

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, IFICDB, IFIPAT, IFIUDB,  
 RTECS\*, TOXCENTER, USPATFULL  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

21 REFERENCES IN FILE CA (1962 TO DATE)  
 21 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:38538  
 REFERENCE 2: 137:363099  
 REFERENCE 3: 137:304801  
 REFERENCE 4: 136:406875  
 REFERENCE 5: 136:241691  
 REFERENCE 6: 136:226808  
 REFERENCE 7: 135:56081  
 REFERENCE 8: 135:41024  
 REFERENCE 9: 128:303619  
 REFERENCE 10: 128:252536

L60 ANSWER 4 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 7724-40-5 REGISTRY

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-ethoxyoctahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

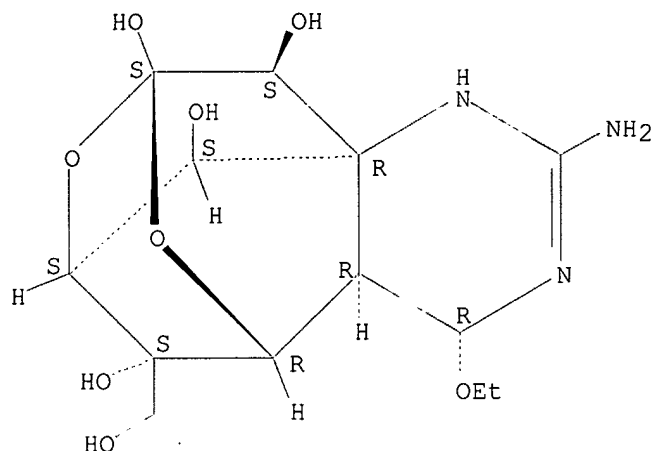
CN Tetrodotoxin, O4-ethyl- (7CI, 8CI)

OTHER NAMES:

CN 4-Ethoxytetrodotoxin

CN Ethoxytetrodotoxin  
 FS STEREOSEARCH  
 DR 16846-39-2  
 MF C13 H21 N3 O8  
 LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, RTECS\*, TOXCENTER, USPATFULL  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

7 REFERENCES IN FILE CA (1962 TO DATE)  
 7 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:363099  
 REFERENCE 2: 137:304801  
 REFERENCE 3: 136:406875  
 REFERENCE 4: 136:241691  
 REFERENCE 5: 136:226808  
 REFERENCE 6: 128:303619  
 REFERENCE 7: 128:252536

L60 ANSWER 5 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 7724-39-2 REGISTRY

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-  
 tetrol, octahydro-12-(hydroxymethyl)-2-imino-4-methoxy-,  
 (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Tetrodotoxin, O4-methyl-

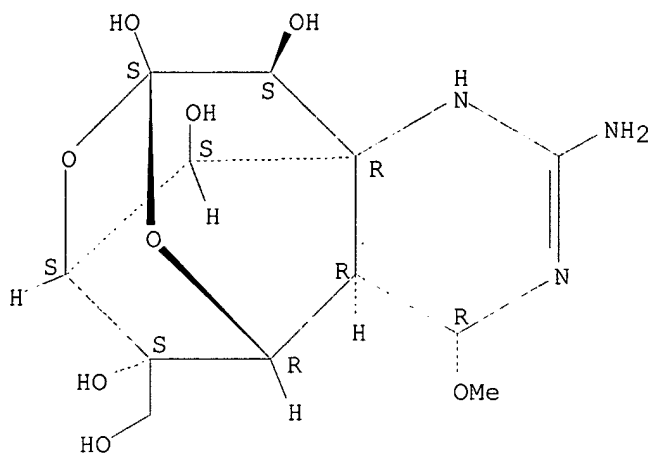
OTHER NAMES:

CN 4-Methoxytetrodotoxin  
 CN 4-O-Methyltetrodotoxin  
 CN Methoxytetrodotoxin  
 FS STEREOSEARCH  
 DR 16846-38-1, 17289-93-9

MF C12 H19 N3 O8

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, RTECS\*, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

7 REFERENCES IN FILE CA (1962 TO DATE)  
 7 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:363099

REFERENCE 2: 137:304801

REFERENCE 3: 136:406875

REFERENCE 4: 136:241691

REFERENCE 5: 136:226808

REFERENCE 6: 128:303619

REFERENCE 7: 128:252536

L60 ANSWER 6 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 7724-38-1 REGISTRY

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-7,10,11,12-tetrol, 4-amino-octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Tetrodotoxin, 4-amino-4-deoxy-, (4.alpha.)- (8CI)

OTHER NAMES:

CN 4-Aminodeoxytetrodotoxin

CN Tetrodaminotoxin

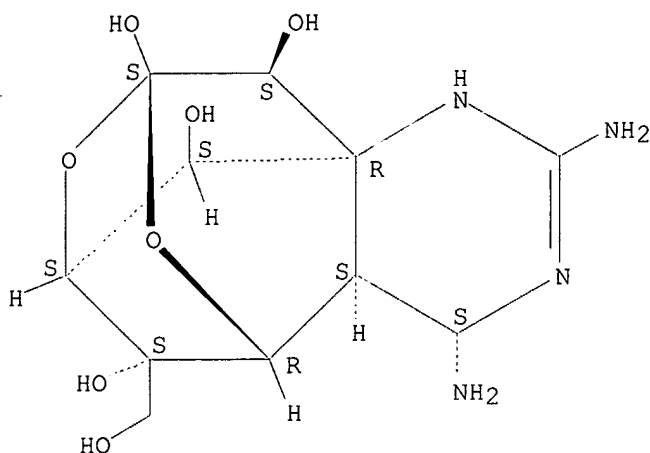
FS STEREOSEARCH

DR 16998-62-2, 17289-94-0, 2054-84-4

MF C11 H18 N4 O7

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, RTECS\*, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

14 REFERENCES IN FILE CA (1962 TO DATE)  
 14 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:363099  
 REFERENCE 2: 137:304801  
 REFERENCE 3: 136:406875  
 REFERENCE 4: 136:241691  
 REFERENCE 5: 136:226808  
 REFERENCE 6: 128:252536  
 REFERENCE 7: 121:99052  
 REFERENCE 8: 67:89145  
 REFERENCE 9: 65:13482  
 REFERENCE 10: 65:13481

L60 ANSWER 7 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 4368-28-9 REGISTRY

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, (4R,4aR,5R,7S,9S,10S,10aR,11S,12S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 8a(1H)-Quinazolineorthoglycolic acid, octahydro-4,5,6,7,8-pentahydroxy-6-(hydroxymethyl)-2-imino-, cyclic 8a,5:8a,7-ester (7CI)

CN Tetrodotoxin (8CI)

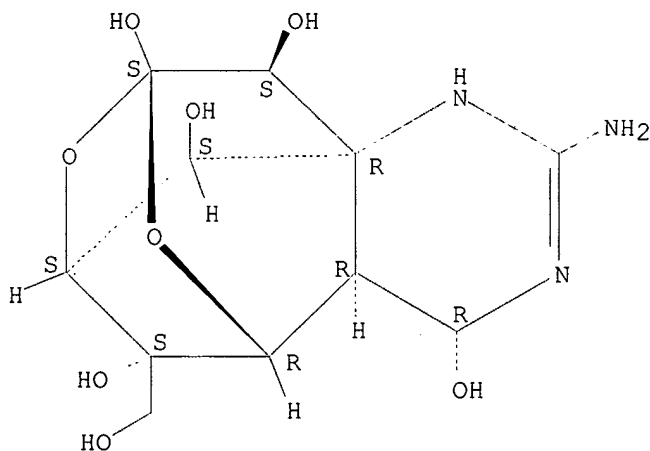
OTHER NAMES:

CN (-)-Tetrodotoxin

CN 5,9:7,10a-Dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol, octahydro-12-(hydroxymethyl)-2-imino-, [4R-(4.alpha.,4a.alpha.,5.alpha.,7.alpha.,9.alpha.,10.alpha.,10a.beta.,11S\*,12

S\*)]-  
 CN Araregai toxin  
 CN Babylonia japonica toxin 1  
 CN BJT 1  
 CN Maculotoxin  
 CN Spheroidine  
 CN Tarichatoxin  
 CN Tetrodotoxine  
 CN TTX  
 CN [4R-(4.alpha.,4a.alpha.,5.alpha.,7.alpha.,9.alpha.,10.alpha.,10a.beta.,11S\*,12S\*)]-Octahydro-12-(hydroxymethyl)-2-imino-5,9:7,10a-dimethano-10aH-[1,3]dioxocino[6,5-d]pyrimidine-4,7,10,11,12-pentol  
 FS STEREOSEARCH  
 DR 12626-86-7, 9014-39-5, 11005-69-9, 11026-09-8, 17289-88-2, 2229-61-0  
 MF C11 H17 N3 O8  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB\*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, NAPRALERT, NIOSHTIC, PROMT, RTECS\*, TOXCENTER, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2153 REFERENCES IN FILE CA (1962 TO DATE)  
 32 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 2153 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:119602  
 REFERENCE 2: 138:118729  
 REFERENCE 3: 138:86718  
 REFERENCE 4: 138:83723  
 REFERENCE 5: 138:69369



REFERENCE 6: 138:69322

REFERENCE 7: 138:68171

REFERENCE 8: 138:68040

REFERENCE 9: 138:49952

REFERENCE 10: 138:38538

L60 ANSWER 8 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 3270-35-7 REGISTRY

CN 1H-4,8a-(Epoxyethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, (4S,4aR,5R,6S,7R,8R,8aR,9R)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

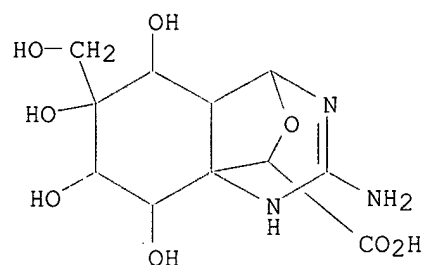
CN 1H-4,8a-(Epoxyethano)quinazoline-9-carboxylic acid, 2-amino-4,4a,5,6,7,8-hexahydro-5,6,7,8-tetrahydroxy-6-(hydroxymethyl)-, [4S-(4.alpha.,4a.beta.,5.alpha.,6.beta.,7.beta.,8.beta.,8a.alpha.,9S\*)]-

CN Tetrodonic acid (7CI, 8CI)

MF C11 H17 N3 O8

CI COM

LC STN Files: BEILSTEIN\*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, MEDLINE, NAPRALERT, RTECS\*, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

29 REFERENCES IN FILE CA (1962 TO DATE)

29 REFERENCES IN FILE CAPLUS (1962 TO DATE)

5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:363099

REFERENCE 2: 137:304801

REFERENCE 3: 137:1763

REFERENCE 4: 136:406875

REFERENCE 5: 136:241691

REFERENCE 6: 136:226808

REFERENCE 7: 135:18727

REFERENCE 8: 133:359932

REFERENCE 9: 131:154655

REFERENCE 10: 128:303619

L60 ANSWER 9 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 437-38-7 REGISTRY

CN Propanamide, N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Propionanilide, N-(1-phenethyl-4-piperidyl)- (7CI, 8CI)

OTHER NAMES:

CN 1-Phenethyl-4-(N-phenylpropionamido)piperidine

CN 1-Phenethyl-4-N-propionylanilinopiperidine

CN Durogesic

CN Fentanest

CN Fentanil

CN Fentanyl

CN N-[1-(2-Phenylethyl)-4-piperidinyl]propionanilide

CN Phentanyl

CN R 4263

FS 3D CONCORD

DR 80832-90-2

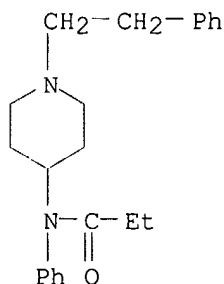
MF C22 H28 N2 O

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, HODOC\*, HSDB\*, IFICDB, IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS\*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU  
(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2763 REFERENCES IN FILE CA (1962 TO DATE)

80 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

2768 REFERENCES IN FILE CAPLUS (1962 TO DATE)

20 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:142483

REFERENCE 2: 138:142316

REFERENCE 3: 138:130907

REFERENCE 4: 138:130900

REFERENCE 5: 138:130394  
 REFERENCE 6: 138:127066  
 REFERENCE 7: 138:117582  
 REFERENCE 8: 138:117574  
 REFERENCE 9: 138:117555  
 REFERENCE 10: 138:112472

L60 ANSWER 10 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 76-99-3 REGISTRY

CN 3-Heptanone, 6-(dimethylamino)-4,4-diphenyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

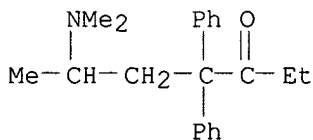
CN (.+-.)-Methadone  
 CN 6-Dimethylamino-4,4-diphenyl-3-heptanone  
 CN Algovetin  
 CN Amidone  
 CN Diaminon  
 CN dl-Methadone  
 CN Dolophin  
 CN Eptadone  
 CN Heptadone  
 CN Heptanon  
 CN Heptanon (pharmaceutical)  
 CN Metasedin  
 CN Methadone  
 CN Phenadone  
 CN Physeptone  
 CN Racemic methadone  
 CN Sedo-Rapide  
 FS 3D CONCORD  
 DR 297-88-1  
 MF C21 H27 N O  
 CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HODOC\*, HSDB\*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, NIOSHTIC, PHARMASEARCH, PROMT, RTECS\*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2333 REFERENCES IN FILE CA (1962 TO DATE)  
 46 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 2338 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:118594  
REFERENCE 2: 138:117520  
REFERENCE 3: 138:112555  
REFERENCE 4: 138:102127  
REFERENCE 5: 138:102125  
REFERENCE 6: 138:101312  
REFERENCE 7: 138:100807  
REFERENCE 8: 138:95716  
REFERENCE 9: 138:84582  
REFERENCE 10: 138:49798

L60 ANSWER 11 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 76-57-3 REGISTRY

CN Morphinan-6-ol, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-,  
(5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Morphinan-6.alpha.-ol, 7,8-didehydro-4,5.alpha.-epoxy-3-methoxy-17-methyl-  
(8CI)

OTHER NAMES:

CN (-)-Codeine

CN Codeine

CN Codicept

CN Coducept

CN 1-Codeine

CN Methyilmorphine

CN Morphine 3-methyl ether

CN Morphine monomethyl ether

CN O3-Methyilmorphine

FS STEREOSEARCH

DR 120210-43-7, 79990-78-6

MF C18 H21 N O3

CI COM

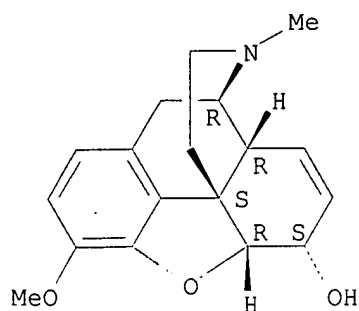
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,  
CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM\*,  
DIOGENES, DRUGU, EMBASE, GMELIN\*, HODOC\*, HSDB\*, IFICDB, IFIPAT, IFIUDB,  
MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHARMASEARCH, PROMT,  
RTECS\*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4031 REFERENCES IN FILE CA (1962 TO DATE)  
 54 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 4040 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:142593  
 REFERENCE 2: 138:133514  
 REFERENCE 3: 138:132331  
 REFERENCE 4: 138:132330  
 REFERENCE 5: 138:132329  
 REFERENCE 6: 138:132323  
 REFERENCE 7: 138:132315  
 REFERENCE 8: 138:131153  
 REFERENCE 9: 138:118594  
 REFERENCE 10: 138:117574

L60 ANSWER 12 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 57-27-2 REGISTRY

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-  
 (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Morphinan-3,6.alpha.-diol, 7,8-didehydro-4,5.alpha.-epoxy-17-methyl- (8CI)

OTHER NAMES:

CN (-)-Morphine

CN Dulcontin

CN Duromorph

CN l-Morphine

CN Meconium

CN Morphia

CN Morphin

CN Morphina

CN Morphine

CN Morphinism

CN Morphinum

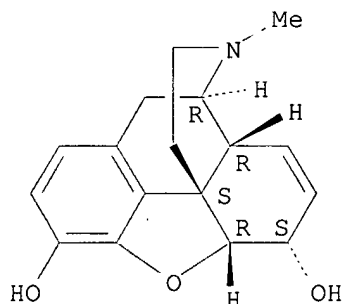
CN Morphium

CN MS Contin

CN Nepenthe

CN Ospalivina  
FS STEREOSEARCH  
DR 8053-16-5, 85201-37-2, 47106-99-0  
MF C17 H19 N O3  
CI COM  
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*,  
BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT,  
CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU,  
DETERM\*, DIOGENES, DRUGU, EMBASE, GMELIN\*, HODOC\*, HSDB\*, IFICDB,  
IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC,  
PHAR, PHARMASEARCH, PIRA, PROMT, RTECS\*, SPECINFO, TOXCENTER, USAN,  
USPAT2, USPATFULL, VETU  
(\*File contains numerically searchable property data)  
Other Sources: EINECS\*\*  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

20056 REFERENCES IN FILE CA (1962 TO DATE)  
241 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
20082 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:142593  
REFERENCE 2: 138:142316  
REFERENCE 3: 138:137023  
REFERENCE 4: 138:133514  
REFERENCE 5: 138:133007  
REFERENCE 6: 138:132508  
REFERENCE 7: 138:132330  
REFERENCE 8: 138:132329  
REFERENCE 9: 138:132328  
REFERENCE 10: 138:132324

L60 ANSWER 13 OF 13 REGISTRY COPYRIGHT 2003 ACS

RN 52-26-6 REGISTRY

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-  
(5.alpha.,6.alpha.)-, hydrochloride (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Morphinan-3,6.alpha.-diol, 7,8-didehydro-4,5.alpha.-epoxy-17-methyl-, hydrochloride (8CI)

## OTHER NAMES:

CN (-)-Morphine hydrochloride

CN Ampek

CN Epimore

CN Morphine chlorhydrate

CN Morphine hydrochloride

CN Theba-Intran

CN Thebametten

FS STEREOSEARCH

MF C17 H19 N O3 . Cl H

CI COM

LC STN Files: ADISINSIGHT, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSNB, DETHERM\*, DIOGENES, EMBASE, GMELIN\*, HSDB\*, IPA, MRCK\*, NIOSHTIC, PROMT, RTECS\*, TOXCENTER, USAN, USPATFULL

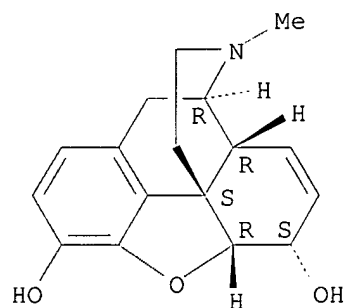
(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

CRN (57-27-2)

Absolute stereochemistry. Rotation (-).



● HCl

1438 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1438 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:130962

REFERENCE 2: 138:130903

REFERENCE 3: 138:100947

REFERENCE 4: 138:61304

REFERENCE 5: 138:49892

REFERENCE 6: 138:33188

REFERENCE 7: 138:29052

REFERENCE 8: 137:379912

REFERENCE 9: 137:363099

REFERENCE 10: 137:315958

=> fil wpix  
FILE 'WPIX' ENTERED AT 10:28:13 ON 05 MAR 2003  
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FILE LAST UPDATED: 3 MAR 2003 <20030303/UP>  
MOST RECENT DERWENT UPDATE: 200315 <200315/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> SLART (Simultaneous Left and Right Truncation) is now  
available in the /ABEX field. An additional search field  
/BIX is also provided which comprises both /BI and /ABEX <<<

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[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

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=> d all abeq tech abex tot

L123 ANSWER 1 OF 2 WPIX (C) 2003 THOMSON DERWENT

AN 2003-140323 [13] WPIX

DNC C2003-035545

TI ~~New composition~~ useful for producing analgesia in a mammal for treating  
e.g. chronic or acute pain, comprises an opioid e.g. **morphine**, a  
sodium channel blocker e.g. **tetrodotoxin**, and a carrier.

DC B05

IN ~~KU, B; SHUM, F. H. K.~~

PA (WEXM-N) WEX MEDICAL INSTR CO LTD

CYC 100

PI WO 2002094272 A1 20021128 (200313)\* EN 18p A61K031-517

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM  
ZW

ADT WO 2002094272 A1 WO 2002-CN339 20020520

PRAI CN 2001-118098 20010518

IC ICM A61K031-517

ICS A61K031-485; A61P025-04



AB WO 200294272 A UPAB: 20030224

NOVELTY - New composition comprises:

- (1) an opioid (a);
- (2) a sodium channel blocker (b) that binds to the SS1 or SS2 subunit of a sodium channel; and
- (3) a carrier (c).

ACTIVITY - Analgesic; Cytostatic; Osteopathic; Tranquilizer.

MECHANISM OF ACTION - Pain inhibitor; Sodium channel blocker; Opioid agonist.

A test was performed to evaluate pain inhibition. Wistar male rats with a body weight of 180-300 g were dosed intramuscularly. Normal saline was used as control, TTX (0.39 micro g/kg) co-administered with **morphine** (0.19 micro g/kg), in a volume of 0.1 ml/100 g body weight. The assay was performed according to the method described in Voges et al..

The medium inhibition dose, ID50 was determined and was found to be 66.2.

USE - For producing analgesia in a mammal (claimed) for treating chronic or acute pain, bone degenerative diseases and cancer. (a) can also be used to achieve a depressive effect on the central nervous system.

ADVANTAGE - Co-administering opioids (a) and sodium channel blocker (b) produces analgesia and results in a greater-than-additive effect.

Dwg.0/5

FS CPI

FA AB; DCN

MC CPI: B04-A04; B06-D17; B06-E05; B07-D05; B14-C01; B14-H01B; B14-J01B; B14-N01

TECH UPTX: 20030224

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The compound that binds to the SS1 or SS2 subunit of a sodium channel is

**tetrodotoxin** (preferably octahydro-12-(hydroxymethyl)-2-imino-5,9:7,10a-dimethano-10aH-(1,3)dioxocino(6,5-d)pyrimidine-4,7,10,11,12-pentol) or its derivatives or **saxitoxin** (preferably 2,6-diamino-4-((aminocarbonyl)oxy)methyl-3a,4,8,9-tetrahydro-1H,10H-pyrrolo(1,2-c)purine-10,10-diol(3aS-(3a-a-a-4-a,10aR asterisk)) or its salts.

(b) is at least one selected from **tetrodotoxin** (TTX), **anhydrotetrodotoxin**, **tetrodaminotoxin**, **methoxytetrodotoxin**, **ethoxytetrodotoxin**, **deoxytetrodotoxin** or **tetradonic acid**.

The **saxitoxin** comprises a tetrahydropurine moiety composed of two guanidine units fused together in a stable azaketall linkage, having a molecular formula C10H17N7O4.

Preferred Composition: The ratio of (b):(a) is 1:100-1:30000.

ABEX

SPECIFIC COMPOUNDS - **Morphine**, **codeine**, **methadone** and **fentanyl** are specifically claimed as (a).

ADMINISTRATION - The dosage of **tetrodotoxin** or **saxitoxin** is 0.01-20 microg/kg and the dosage of **morphine** is 0.002-20 mg/kg and administered separately. The administration is intrathecally or intramuscularly (all claimed).

EXAMPLE - No relevant example given.

L123 ANSWER 2 OF 2 WPIX (C) 2003 THOMSON DERWENT

AN 2002-434994 [46] WPIX

DNC C2002-123478

TI Production of analgesia in a mammal experiencing pain e.g. neuropathic pain, cancer pain involves systemic administration of a sodium channel blocking compound e.g. **tetrodotoxin** in a vehicle.

DC B02

IN DONG, Q; SHUM, F H K; SHUM, F H

PA (WEXM-N) WEX MEDICAL INSTR CO; (WEIK-N) WEIKESI MEDICAL INSTR CO LTD;  
(WEXM-N) WEX MEDICAL INSTR CO LTD

CYC 96

PI WO 2002022129 A1 20020321 (200246)\* EN 60p A61K031-517  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM-DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU  
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
US 6407088 B1 20020618 (200248) A61K031-33  
AU 2002013785 A 20020326 (200251) A61K031-517  
CN 1356104 A 20020703 (200265) A61K031-505

ADT WO 2002022129 A1 WO 2001-CN1391 20010911; US 6407088 B1 US 2000-695053  
20001025; AU 2002013785 A AU 2002-13785 20010911; CN 1356104 A CN  
2000-124517 20000918

FDT AU 2002013785 A Based on WO 200222129

PRAI CN 2000-124517 20000918

IC ICM A61K031-33; A61K031-505; A61K031-517

ICS A61K031-44; A61P023-02; A61P025-04

AB WO 200222129 A UPAB: 20020722

NOVELTY - Production of analgesia in a mammal experiencing pain involves systemic administration of a sodium channel blocking compound (I) in a vehicle.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a kit comprising a composition (compound (I) and a carrier), and a written material describing systemic administration of the composition for the treatment of pain.

ACTIVITY - Analgesic.

Wister rats (180 - 240 g, half of each sex) were randomly divided into **tetrodotoxin** (TTX)-tested groups, positive control groups (aspirin or meperidine) and negative control group (normal saline (NS)). The mice were fasted for 12 hours before the test, and allowed to drink ad-libitum. TTX was given subcutaneously or intramuscularly and 40 minutes later, 0.6% acetic acid (0.1 ml/10 g) was given intraperitoneally as a chemical stimulus. The writhing incidence in the mice was observed and was recorded within the following 15 minutes. The mice in NS group, aspirin group and Meperidine groups were treated the same way. The writhing incidences in the TTX groups were compared to the control group and ID50 was calculated. The ID50 in the TTX, aspirin and meperidine treated mice was found to be: 2.68 micro g/kg, 198.8 mg/kg and 1.8 mg/kg, respectively. Thus the analgesic effect of TTX was much stronger than of aspirin and was 670 times stronger than meperidine. The analgesic potency of TTX was also found to be similar in different routes of administration.

MECHANISM OF ACTION - Sodium channel blocker.

USE - For producing analgesia in a mammal experiencing pain caused by mechanical, chemical, or ischemic stimulation, or inflammation, neuropathic pain, and pain arising from cancer such as liver, rectal, bone, lymphatic, esophageal, genital organs, prostate, digestive system, stomach, colon, breast, respiratory system, lung, bronchial, urinary, skin cancer, lymphoma, leiomyosarcoma (all claimed), central pain, and phantom limb pain.

ADVANTAGE - The sodium channel blocking compound does not cause drug dependence or addiction in the mammal (preferably a female of childbearing age), does not have any non-reversible adverse effect, does not produce local intramuscular irritation at the region where the systemic administration is performed, does not produce any general hypersensitivity reaction in the mammal, and does not induce haemolysis or vascular stimulation in the mammal (claimed).

The short course of treatment of **tetrodotoxin** of only 3 days, as compared to any other strong analgesics that must be administered consistently and continuously to be effective, and thus exhibits considerable advantages over any other of the currently used analgesics.

After administration of the **tetrodotoxin** after 3 days, the analgesic effect lasts for 20 - 30 days. **Tetrodotoxin** also produced evident detoxification in the patients who were dependent on dolantin.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B06-D17; B06-E05; B14-C01; B14-L06

TECH UPTX: 20020722

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The composition comprises an acetic acid solution of **tetrodotoxin** when the administration is by injection.

Preferred Compound: (I) has a tetrahydropurine moiety comprising two guanidine units fused together in a stable azaketal linkage, having a molecular formula  $C_{10}H_{17}N_7O_4$ , (molecular weight = 299.30), or its derivative.

ABEX

SPECIFIC COMPOUNDS - **Tetrodotoxin**, **anhydrotetrodotoxin**, **tetradaminotoxin**, **methoxytetrodotoxin**, **ethoxytetrodotoxin**, **deoxytetrodotoxin**, **tetrodonic acid**, **hydroxysaxitoxin**, and **neosaxitoxin** are specifically claimed as (a).

ADMINISTRATION - (I) is administered systematically (by intramuscular injection, subcutaneous injection, intravenous injection), orally, sublingually, skin patch, implantable osmotic pump, collagen implant, aerosol inhalation, or suppository. The dosage is (0.1 - 5) mug/kg body weight at least once (preferably every 3 - 12 hours during a treatment period of 1 - 10 (preferably 3) days) in a repeated treatment (claimed).

EXAMPLE - A 44 year old male had developed abdominal pain and was diagnosed with smooth muscle pain in the back wall of his celiac for which he underwent a surgical procedure. One year later, his abdomen pain relapsed and he was operated on again. The pathological examination from the second operation revealed that he had developed a smooth muscle sarcoma (leiomyosarcoma), later finding that his sarcoma had spread to his liver and that he now required and received anti-cancer treatment (chemotherapy). He began to inject dolantin (control) due to the severe pain in his abdomen. He needed to inject dolantin at least 3 times per day. Initially he was taking the dolantin by intramuscular injection, and finally he needed to use intravenous injection in order to have the dolantin take effect faster. Just prior to when he received the **tetrodotoxin** (test) treatment, he had taken over 100 injections of dolantin in the previous month. At the beginning, when he stopped using dolantin, he experienced **morphine**-like withdrawal symptoms, such as whole body weakness and pain, trembling when standing up and difficulty walking. He voluntarily received **tetrodotoxin** treatment. His pain intensity was severe before using **tetrodotoxin**. 5 minutes after the first injection of **tetrodotoxin**, the pain was completely disappeared. After 3 days of treatment, the patient was able to live normally and continue to feel comfortable without any pain.

=> d his

(FILE 'HOME' ENTERED AT 09:22:31 ON 05 MAR 2003)  
SET COST OFF

FILE 'REGISTRY' ENTERED AT 09:22:41 ON 05 MAR 2003

L1 4 S (MORPHINE OR CODEINE OR METHADONE OR FENTANYL)/CN  
L2 7 S (SAXITOXIN OR TETRODONIC ACID OR ETHOXYTETRODOTOXIN OR TETROD  
E TTRODIAMINOTOXIN  
E TDTRODIAMINOTOXIN

E TETRODIAMINOTOXIN  
E TETRADIAMINOTOXIN

FILE 'HCAPLUS' ENTERED AT 09:24:41 ON 05 MAR 2003

L3 25258 S L1  
L4 43711 S MORPHINE OR CODEINE OR METHADONE OR METADONE OR FENTANYL  
L5 44759 S L3,L4  
L6 2764 S L2  
L7 11980 S SAXITOXIN OR TETRODONIC ACID OR ETHOXYTETRODOTOXIN OR TETRODO  
L8 0 S ?TETRODIAMINOTOXIN?  
L9 0 S ?DIAMINOTOXIN?  
L10 0 S ?DIAMINODOTOXIN?  
L11 190 S L5 AND L6,L7  
L12 1 S L11 AND (SS1 OR SS2)

FILE 'REGISTRY' ENTERED AT 09:27:03 ON 05 MAR 2003

L13 1 S 7724-38-1

FILE 'HCAPLUS' ENTERED AT 09:27:17 ON 05 MAR 2003

L14 16 S L13  
L15 0 S TETRODIAMINOTOXIN  
L16 14 S TETRODAMINOTOXIN  
L17 1 S L14,L15 AND L5  
L18 1 S L12,L17  
L19 1 S L18 AND L3-L12,L14-L18

FILE 'REGISTRY' ENTERED AT 09:28:16 ON 05 MAR 2003

SEL RN L1  
L20 432 S E1-E4/CRN  
L21 8 S L2,L13  
SEL RN  
L22 85 S E5-E12/CRN  
L23 0 S L20 AND L22

FILE 'HCAPLUS' ENTERED AT 09:28:41 ON 05 MAR 2003

L24 5564 S L20  
L25 45130 S L5,L24  
L26 55 S L22  
L27 12078 S L6,L7,L14,L16,L26  
L28 191 S L25 AND L27  
L29 1 S L28 AND (SS1 OR SS2)  
E ION CHANNEL/CT  
E E34  
L30 1559 S E3  
E ION CHANNEL/CT  
E E27+ALL  
L31 893 S E4 (L) SODIUM  
L32 75 S E4 (L) (SS1 OR SS2 OR SUBTYP? OR SUBUNIT?)  
L33 0 S L28 AND L30  
L34 2 S L28 AND L31  
L35 0 S L28 AND L32  
L36 125 S L28 AND (SYNERG? OR MIX? OR FORMUL? OR COMBIN? OR COMPOSITION  
L37 11 S L36 AND (NA OR SODIUM) (L)CHANNEL?  
L38 40 S L3,L24 AND L6,L14,L26  
L39 40 S L38 AND L28-L37  
L40 94 S L36 NOT L37-L39  
L41 3 S L40 AND (OPPOSITE OR ATTENUAT?)/TI  
L42 49 S L28 NOT L36-L41  
E KU B/AU  
L43 45 S E3-E9  
E SHUM F/AU  
L44 9 S E3,E8,E10  
E KONG F/AU

E KONG FRANK/AU  
 E KONG S/AU  
 E KONG SHUM/AU  
 L45 6 S L43,L44 AND L25-L27  
 L46 32 S (SHUM H? OR SHUM F?)/AU  
 L47 7 S L46 AND L25-L27  
 L48 8 S L45,L47  
 L49 5 S L48 NOT (EXTRACT? OR PURIF?)/TI  
 L50 6 S L34,L49 AND L3-L12,L14-L19,L24-L49  
 L51 14352 S L27 OR L30 OR L31 OR L32  
 L52 8935 S (NA OR SODIUM) (L) CHANNEL?(L) BLOCK?  
 L53 52 S L52 AND L25  
 L54 119 S L52 AND (NARCOTIC OR OPIOID OR OPIATE)  
 L55 142 S L53,L54  
 L56 128 S L55 NOT L36-L42,L11  
 L57 48 S L56 AND ION CHANNEL?/CT  
 SEL DN AN 9 42  
 L58 2 S E1-E6  
 L59 8 S L50,L58 AND L3-L12,L14-L19,L24-L58  
 SEL HIT RN

FILE 'REGISTRY' ENTERED AT 09:53:22 ON 05 MAR 2003

L60 13 S E7-E19

FILE 'HCAPLUS' ENTERED AT 09:53:57 ON 05 MAR 2003

FILE 'REGISTRY' ENTERED AT 09:54:14 ON 05 MAR 2003

FILE 'EMBASE' ENTERED AT 09:54:28 ON 05 MAR 2003

L61 69876 S L1  
 L62 55692 S L20  
 L63 69876 S (MORPHINE OR CODEINE OR METHADONE OR FENTANYL)/CT  
 E OPIOID/CT  
 E E3+ALL  
 E E2+ALL  
 L64 18143 S E1+NT  
 E NARCOTIC/CT  
 E E7+ALL  
 L65 102041 S E4+NT  
 L66 110189 S L61-L65  
 L67 13460 S L21 OR L22  
 L68 16054 S L7 OR L16  
 L69 16054 S L67,L68  
 E SODIUM CHANNEL/CT  
 E E4+ALL  
 L70 3133 S E4+NT  
 L71 1958 S E7+NT  
 L72 474 S L66 AND L69  
 L73 117 S L66 AND L70  
 L74 182 S L66 AND L71  
 L75 659 S L72-L74  
 E DRUG SYNERG/CT  
 E E4+ALL  
 E E2+ALL  
 L76 18 S E1+NT AND L75  
 L77 8338 S L66 (L) CB/CT  
 L78 29 S L77 AND L75  
 L79 192 S L69-L71 (L) CB/CT  
 L80 16 S L79 AND L75  
 L81 33 S L78,L80  
 L82 6 S L81 NOT AB/FA  
 L83 27 S L81 NOT L82

FILE 'CANCERLIT' ENTERED AT 10:15:43 ON 05 MAR 2003

L84 2284 S L1 OR L20  
L85 3492 S L4  
L86 3492 S L84-L85  
L87 276 S L21 OR L22  
L88 452 S L7 OR L16  
L89 452 S L87,L88  
L90 2 S L86 AND L89

FILE 'MEDLINE' ENTERED AT 10:17:00 ON 05 MAR 2003

L91 50827 S L86  
L92 14592 S L89  
L93 180 S L91 AND L92  
L94 38 S L93 NOT AB/FA  
E SYNERG/CT  
E E6+ALL  
E E2+ALL  
L95 40145 S E4+NT  
E E3+ALL  
E DRUG COMBINATION/CT  
L96 34928 S E6+NT  
E DRUG THERAPY, COMBINED/CT  
E DRUG THERAPY, COMBINATION/CT  
L97 72221 S E3+NT  
L98 9 S L93 AND L95-L97

FILE 'WPIX' ENTERED AT 10:20:48 ON 05 MAR 2003

L99 2313 S L4/BIX  
E MORPHINE/DCN  
E E3+ALL  
L100 668 S E2 OR 0127/DRN  
L101 214 S E4  
L102 2 S E6  
L103 39 S E8  
L104 81 S E14  
E CODEINE/DCN  
E E3+ALL  
L105 374 S E2 OR 0405/DRN  
L106 137 S E4  
L107 48 S E8  
L108 11 S E10  
E METHADONE/DCN  
E E3+ALL  
L109 185 S E2 OR 0408/DRN  
L110 6 S E4  
E FENTANYL/DCN  
E E3+ALL  
L111 252 S E2 OR 1254/DRN  
L112 128 S E4  
L113 20 S E6  
L114 2645 S L99-L113  
L115 75 S L7/BIX OR L16/BIX  
E SAXITOXIN/DCN  
E E3+ALL  
L116 17 S E2  
E TETRODONIC ACID/DCN  
E ETHOXYTETRODOTOXIN/DCN  
E TETRODOTOXIN/DCN  
E E3+ALL  
L117 19 S E2  
E ANHYDROTETRODOTOXIN/DCN  
E TETRODAMINOTOXIN/DCN  
E METHOXYTETRODOTOXIN/DCN

E DEOXYTETRODOTOXIN/DCN  
L118 80 S L115-L117  
L119 4 S L114 AND L118  
SEL DN AN 1 2  
L120 2 S L119 AND E1-E4  
L121 660 S A61K031-485/IC, ICM, ICS, ICA, ICI  
L122 1 S L121 AND L118  
L123 2 S L120, L122

FILE 'WPIX' ENTERED AT 10:28:13 ON 05 MAR 2003

FILE 'DPCI' ENTERED AT 10:28:34 ON 05 MAR 2003  
E WO2002094272/PN